α-HETEROSUBSTITUTED ALDEHYDES IN ORGANIC SYNTHESIS. ENANTIOSELECTIVE APPROACHES TO NEW ANALOGUES OF MEVINIC ACIDS

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Dedicated to the memory of Professor Otakar Červinka, a pioneer in asymmetric synthesis and a good friend.

Various aldol approaches towards the asymmetric synthesis of the lactone moiety of HMG-CoA-reductase inhibitors are described. Auxiliary controlled as well as catalytic aldol reactions resulted only in modest to low selectivities, whereas 1,2-additions to readily available highly enantiomerically enriched α-heterosubstituted aldehydes yielded δ-hydroxy-β-ketoesters with a high degree of diastereocontrol and in good chemical yields. The novel mevinic acid analogues could then be obtained by *syn*-reduction of the addition products.
Keywords: Aldol reactions; Amino aldehydes; Mukaiyama reaction; Stereoselective reactions; Asymmetric synthesis; TADDOL; SAMP; Lactones; HMG-CoA-reductase inhibitors.

Since the link between abnormally high levels of plasma cholesterol (*i.e.* LDL) and coronary heart disease is well established, the search for new drugs to treat hypercholesterolemia and atherosclerosis is an ongoing field of pharmaceutical interest[1]. The following approaches to affect plasma cholesterol are currently being pursued: First: keeping a strict diet, thus affecting the exogenic cholesterol taken up by nutrients. Second: antagonising the *in vivo* biosynthesis of endogenic cholesterol, which represents up to 70% of body cholesterol.

The complex endogenic pathway involves among others the following three key enzymes: HMG-CoA reductase (HMGR)[2], squalene synthase (SQS)[3] and squalene epoxidase (SQE)[4]. Furthermore, most recently interest has been focused on the activity of certain plasma factors (*i.e.* cholesterol ester transfer protein CETP and phospholipid transfer protein PLTP)[5] be-

cause of their ability to control the crucial size distribution of lipoproteins, thus affecting the ratio of LDL to HDL in the plasma.

Although HMGR inhibitors (statins) are still proving to be the most clinically effective therapeutic agents in the treatment of hypercholesterolemia (*e.g.* Mevacor, Lipitor and Crestor), one has to keep in mind that inhibition of cholesterol biosynthesis at an early stage also affects other biologically important pathways. Furthermore, apart from the side effects observed with Baycol in the clinic, which led to its withdrawal from the market, only few side effects like hypertension[6] and myopathy[7] as well as apoptosis of rat hepatocytes[8] are known to date.

Since the lactone portion of synthetic HMGR inhibitors like Fluvastatin[9] exhibit only two stereogenic centers, extensive synthetic studies have been carried out concerning methodology to generate this fragment in enantiomerically pure form[10].

In the present paper we wish to describe in detail our efforts to synthesise the lactone part of HMGR inhibitors *via* various asymmetric aldol approaches[11].

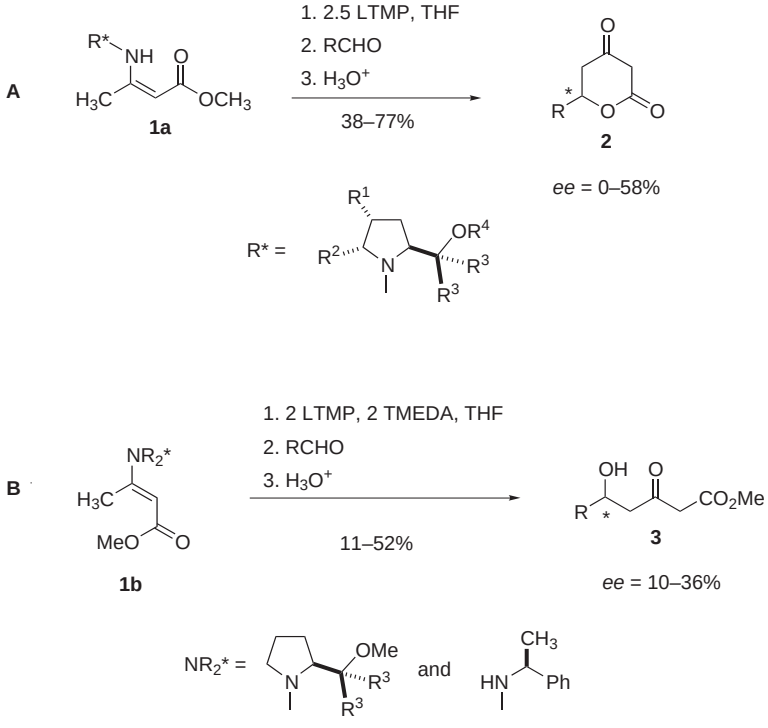
Auxiliary Controlled Asymmetric Aldol Reactions

At the beginning of our studies we intended to build up the lactone portion of HMGR inhibitors *via* a diastereoselective aldol approach[12] using various enantiopure hydrazine and amine auxiliaries[13] as shown in Scheme 1.

Thus, enantiopure methyl acetoacetate derivatives[14] **1a** were deprotonated, employing lithium 2,2,6,6-tetramethylpiperidide (LTMP), and subsequently reacted with various aldehydes. Extensive optimisations involving *inter alia* solvent effects, use of various other bases as well as additives, reaction temperature and duration were pursued, and we observed, after hydrolytic cleavage of the auxiliary (SAMP; R^1, R^2 = H, R^3 = H, R^4 = Me), enantioselectivities of the corresponding tetrahydropyran-2,4-diones **2** in the range of 0 to 58% ee, depending strongly on the steric bulk of the aldehyde (R = *t*-Bu, 58% ee; R = i-Pr, 10% ee; R = Bu, 0% ee). Furthermore, the methoxymethyl-side chain of the chiral auxiliary seems to have exhibited optimal chelation abilities. Exchanging the methyl ether to the free alcohol (R^4 = H) or a silyl ether (R^4 = *tert*-butyldimethylsilyl) as well as introducing more steric bulk into the side chain (R^3 = Me, Et) resulted in a sharp decrease in selectivity. It is interesting to note in this context that in pyruvate-aldol reactions excellent selectivities were obtained with SAEP (R^1, R^2 = H, R^3 = Et, R^4 = Me) as the chiral auxiliary[13b]. However, there is no such trend in β-ketoester aldol reactions. In case of the synthetically more important

dihydrocinnamon aldehyde (R = $PhCH_2CH_2$) it turned out, that the maximum value of 33% ee was found for (*R*,*R*,*R*)-1-amino-2-(methoxymethyl)-1-azabicyclo[3.3.0]octane (R^1, R^2 = $-(CH_2)_3-$, R^3 = H, R^4 = Me) as chiral auxiliary[15]. This result clearly indicates that steric bulkiness on the d-face of the pyrrolidine ring by ring fusion of a cyclopentane moiety has a beneficial effect to the diastereoselectivity of the aldol addition[16]. Interestingly, changing the auxiliary from SAMP to (*S*,*S*)-1-amino-2,5-bis(methoxymethyl)piperidine (C_2-symmetry of the auxiliary) only resulted in a decreased selectivity.

Diastereoselective aldol reactions



SCHEME 1

Employing chiral secondary amines as auxiliaries[13d–13h] (Scheme 1), the aldol reaction of the corresponding metallated enamines **1b** proceeded without concomitant lactonisation, resulting in δ-hydroxy-β-ketoesters **3** with enantioselectivities in the range of ee = 0% (R = Bu) to ee = 36% (R = *t*-Bu).

The use of 2 equivalents LDA proved to be essential to gain maximum selectivity whereas only modest chemical yields (20–67%) due to retro-aldol reactions could be obtained. SMP (R^3 = H) yielded the best ee value, whereas an increasing steric demand in the side chain (R^3 = Me, Et) resulted in lower enantioselectivities again (see above; ee = 10 and 0%, respectively) in case of pivalaldehyde. Interestingly in this context, working on propionate aldol reactions, Schlessinger *et al.* have described excellent diastereoselectivities by using the non-chelating 2,5-dimethylpyrrolidine as the chiral auxiliary[13g]. Finally, using the conditions in Scheme 1B, (*R*)-(+)-1-phenylethylamine yielded maximum selectivities of 56% ee in case of the sterically most demanding pivalaldehyde (R = *t*-Bu), whereas dihydrocinnamon aldehyde (R = $PhCH_2CH_2$) only resulted in 5% enantioselectivity.

Further experiments included the use of titanium and boron enolates ($TiCl_4/NEt_3$, Cy_2BCl/NEt_3), as well as silylketene acetals (TBSOTf/LDA), but no significant improvement in selectivity could be noted.

Asymmetric Aldol Reactions Using Chiral Titanium Complexes

In the next part of our investigation we assessed the possibility of enantioselective aldol reactions[17], using achiral acetoacetate-d^4-reagents and chiral titanium complexes[18] in two different manners (Scheme 2).

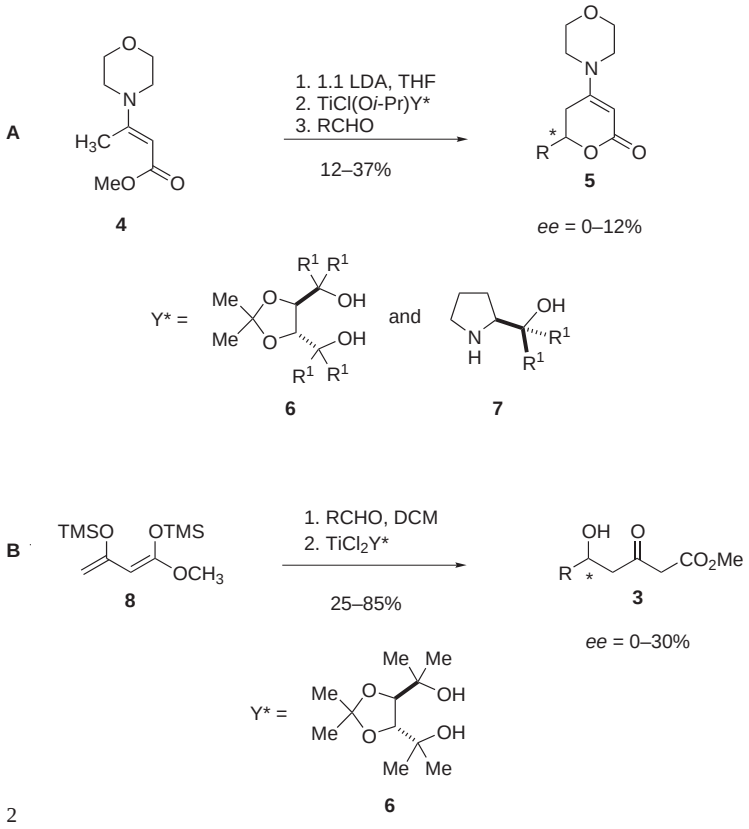
Enantiopure tartarate-based diols (*R*,*R*)-**6** (taddols[19a–19c]) as well as amino alcohols[13b] (*S*)-**7** based on proline were prepared and converted into the corresponding chlorotitanium complexes[19c] to be employed in transmetallations of the lithium enolate of enaminoester[20] **4**. Successive aldol reaction with benzaldehyde yielded β-enaminopyran-2-ones **5** with only low enantioselectivities (ee = 0–12%). Best results were obtained using tetraphenyltaddol (*R*,*R*)-**6** (R^1 = Ph, 10% ee) and SDP (*S*)-**7** (R^1 = Me, 12% ee).

Furthermore, the Mukaiyama aldol reaction of diene[21] **8** with various aldehydes using chiral titanium complexes based on tetraphenyltaddol (*R*,*R*)-**6** resulted in δ-hydroxy-β-ketoesters **3** again with modest selectivities. Interestingly, in the case of hydrocinnamaldehyde ee = 30% was observed, whereas for sterically more hindered aldehydes like pivalaldehyde and benzaldehyde mostly cycloaromatisation of the starting diene was observed and no aldol addition product could be detected. Despite further optimisations like changing the mode of addition and adding tertiary amine bases, we were unable to change the outcome of the reaction.

The recent success of Carreira *et al.*[17d,18f], Sato *et al.*[18k] and Keck *et al.*[18n] based on the use of catalysts with Schiff base and binaphthol ligands shows

that fine tuning of the substitution pattern as well as the donor properties proved to be essential for effective asymmetric catalysis of methyl aldol reactions.

Enantioselective aldol reactions



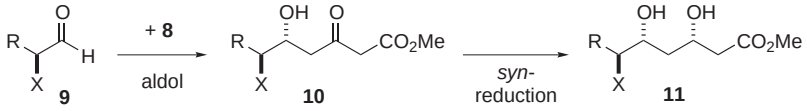
SCHEME 2

Synthesis of α-Heterosubstituted Carbonyl Compounds and Application to the Synthesis of Novel Mevinic Acid Analogues

After the failure of the asymmetric control of methyl aldol reactions, we finally surveyed the possibility of introducing the chirality information into the aldehyde component[22–24] **9** and reacting them with achiral acetoacetate-d^4-reagents. The successive *syn*-reduction of δ-hydroxy-β-ketoester **10** according to Scheme 3 should yield novel mevinic acid analogues **11** with potentially new biological properties in a highly diastereo- and enantioselective manner.

On the other hand, the heterosubstituent X (X = SiR_3, NR_2, SR) may be further manipulated in functional group interconversions as well as in coupling reactions, thus offering a broad synthetic scope.

Diastereoselective 1,2-additions to chiral aldehydes



X = SR, NR_2, SiR_3

SCHEME 3

As we[23a,24b] and Reetz *et al.*[22f] have independently described, optically active α-heterosubstituted aldehydes (X = NR_2, SR, SiR_3 and others) can be efficiently prepared using either the SAMP/RAMP methodology or an ex-chiral pool approach.

Following the precedent of Reetz *et al.*, we obtained α-(dibenzylamino)-substituted aldehydes in three steps with no racemisation (Table I) from commercial α-amino acids. On the other hand, the SAMP/RAMP methodology proved to be the only versatile tool so far to generate α-hetero-

TABLE I
Synthesis of α-(dibenzylamino)-substituted aldehydes

Aldehyde	R	X	*ee*, %
(*S*)-**9a**	i-Pr	NBn_2	≥96
(*S*)-**9b**	*t*-Bu	NBn_2	≥96
(*S*)-**9c**	Bn	NBn_2	≥96
(*S*)-**9d**	i-Bu	NBn_2	≥96
(*S*)-**9e**	Bn	TBDMS	95
(*S*)-**9f**	DCBn[a]	TBDMS	≥92
(*S*)-**9g**	Pr	S*t*-Bu	91
(*S*)-**9h**	i-Pr	S*t*-Bu	91
(*S*)-**9i**	Bn	S*t*-Bu	93
(*S*)-**9j**	DCBn[a]	S*t*-Bu	94
(*S*)-**9k**	Bn	SPh	37[b]
(*S*)-**9l**	i-Pr	SPh	84[b]

[a] DCBn = 2,4-dichlorobenzyl; [b] extensive racemisation during flash chromatography.

substituted carbonyl compounds in a highly enantioselective manner. To this end we were able to extend the methodology to heteroatoms such as sulfur[23a], nitrogen[25a], oxygen[25b], phosphorous[26], silicon[24b] and fluorine[27]. Depending on the tactics employed, both antipodes can be obtained with equal optical purity by using only SAMP as chiral auxiliary. In the outlined publication we only followed the alkylation methodology, incorporating silicon and sulfur as heteroatoms. Thus, 2-heterosubstituted aldehyde-SAMP hydrazones (X = SiR_3, SR) were diastereoselectively alkylated followed by an oxidative cleavage of the chiral auxiliary to yield α-heterosubstituted aldehydes (*S*)-**9a**–(*S*)-**9l** in enantiomerically enriched form[23a,24b,28] (Table I).

2-Phenylsulfanyl substituted aldehydes like (*S*)-**9k** and (*S*)-**9l** proved to be highly prone to racemisation, rendering it necessary to perform the purification by flash chromatography as quickly as possible.

Using (*S*)-2-(dibenzylamino)-4-methylpentanal ((*S*)-**9d**) and various acetoacetate-d^4-reagents, we optimised the aldol reaction conditions as shown in Table II. The initial addition of enaminoester **4** resulted after aqueous work-up in the formation of the corresponding γ-enaminodihydropyran-5-one **5** (Scheme 2A) in only low chemical yield (mostly retro-aldol reaction) and with no diastereocontrol. The dianion of methyl acetoacetate yielded δ-hydroxy-β-ketoester **10d** (Table II, entry 2) with 33% de in favour of the *anti*-addition product. These results could be further improved by employing Mukaiyama aldol reaction conditions for diene **8** (Scheme 2B and Table II, entries 3–5). The simultaneous addition of 2.1 equivalents of titanium tetrachloride and the aldehyde to 3 equivalents of the diene **8** at

TABLE II
Conditions of aldol reaction

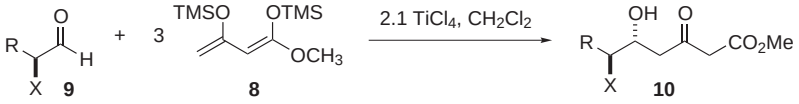
Entry	Acetoacetate-d^4-reagent	Equivalents	Conditions	Yield, %	*de*[a] %
1	**4**	1.0	LDA, THF, –78 °C	4[b]	0
2	methyl-acetoacetate	1.0	NaH, BuLi, THF, –78 °C	80[c]	33
3	**8**	1.0	1.2 $TiCl_2(Oi\text{-}Pr)_2$, DCM, –78 °C	6[c]	≥96
4	**8**	1.0	1.0 $TiCl_4$, DCM, –78 °C	33[c]	≥96
5	**8**	1.0	2.1 $TiCl_4$, DCM, –78 °C	60[c]	97

[a] Determined by ^{13}C NMR; [b] γ-enaminodihydropyran-2-one; [c] δ-hydroxy-β-ketoester.

–78 °C turned out to be high yielding (54–87%) with excellent diastereoselectivities (de > 96%).

Employing these reaction conditions to various enantiomerically enriched aldehydes, we were able to generate a broad range of δ-hydroxy-β-ketoesters **10** with high diastereoselectivities and virtually no loss of enantiomeric purity (Table III).

TABLE III
Preparation of δ-hydroxy-β-ketoesters **10**



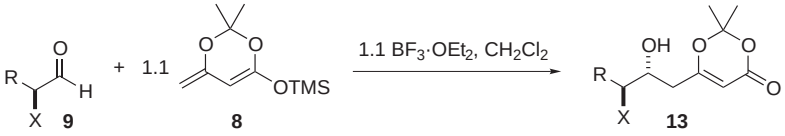
Hydroxyester **10**	Aldehyde R, X	Yield, %	*de*[a], %	*ee*[b], %
(*R*,*S*)-**10a**	i-Pr, NBn_2	60	≥96	≥96
(*R*,*S*)-**10b**	*t*-Bu, NBn_2	71	≥96	≥96
(*R*,*S*)-**10c**	Bn, NBn_2	71	≥96	≥96
(*R*,*S*)-**10d**	i-Bu, NBn_2	70	≥96	≥96
(*R*,*S*)-**10e**	Bn, TBDMS	54	≥96	93
(*R*,*S*)-**10f**	DCBN[c], TBDMS	60	≥96	95
(*R*,*S*)-**10g**	Pr, S*t*-Bu	88	≥96	91
(*R*,*S*)-**10h**	i-Pr, S*t*-Bu	76	≥96	91
(*R*,*S*)-**10i**	Bn, S*t*-Bu	87	≥96	93
(*R*,*S*)-**10j**	DCBn[c], S*t*-Bu	81	≥96	94

[a] Determined by ^{13}C NMR; [b] determined by ^{1}H NMR using (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.); [c] DCBn = 2,4-dichlorobenzyl.

As an alternative methodology we reacted the ketene acetal[29] **8** in Mukaiyama aldol reactions using $BF_3 \cdot OEt_2$ and α-sulfenylated aldehydes to isolate the corresponding *anti*-addition products (*R*,*S*)-**13** after flash chromatography. Herein we observed a crucial dependence of the diastereo as well as the enantio control on the group on sulfur (Tables I and IV).

In a similar study on 1,2-additions to racemic α-sulfenylated aldeyhdes Annunziata *et al.*[23c] found, that diastereoselectivities depended on the Lewis acid and on the group of sulfur employed. They described highest *anti*-selectivities using borontrifluoride etherate whereas titanium tetrachloride resulted in lower *syn*- (S-i-Pr) or *anti*-selectivities (SPh).

TABLE IV
Degrees of *anti*-selectivity of α-heterosubstituted aldehydes[29]



Hydroxylactone	R, X	Yield, %	*de*, %	*ee*, %
(*R*,*S*)-**13i**	Bn, S*t*-Bu	86	92	93
(*R*,*S*)-**13l**	i-Pr, SPh	89	52	80[a]

[a] Extensive racemisation of the aldehyde during work-up.

On the other hand, Sato *et al.*[29b] studied the diastereoselective additions of diene **8** to α-(benzyloxy)-substituted aldehydes and they have found high *syn*-selectivities using titanium tetrachloride as the Lewis acid.

Looking at our results, we were pleased to find high *anti*-selectivities throughout the whole range of α-heterosubstituted aldehydes with titanium tetrachloride as the Lewis acid (Table III). The Grunwell protocol[29], however, did not result in equally consistent degrees of *anti*-selectivity (Table IV). We therefore conclude that the selectivity is determined solely by the chelation abilities of the heterosubstituent and not by the Lewis acid employed.

TABLE V
Preparation of *syn*-3,5-dihydroxyesters (*S*,*R*,*S*)-**11**

syn-Dihydroxyester	Yield, %	*de*[a], %	*ee*, %
(*S*,*R*,*S*)-**11a**	67	≥96	≥96
(*S*,*R*,*S*)-**11b**	51	≥96	≥96
(*S*,*R*,*S*)-**11c**	61	≥96	≥96
(*S*,*R*,*S*)-**11e**	55	≥96	93
(*S*,*R*,*S*)-**11f**	52	≥96	95
(*S*,*R*,*S*)-**11i**	78	80[b]	93
(*S*,*R*,*S*)-**11j**	86	80[b]	94

[a] In crude product determined by ^{13}C NMR; [b] after recrystalisation from pentane determined by ^{13}C NMR.

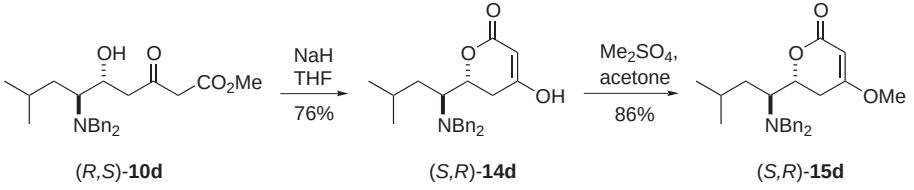
With the δ-hydroxy-β-ketoesters (*R*,*S*)-**10** in hand, we then performed the *syn*-reduction of the ketone moiety. The conditions of Narasaka *et al.*[30a], later modified by Sletzinger *et al.*[30b], found widespread applications in the literature and proved to be a powerful tool to introduce the required *syn*-diol functionality.

Thus, treatment of the δ-hydroxy-β-ketoesters with 1.2 equivalents of tributylborane and catalytic amounts of pivalic acid in tetrahydrofuran followed by addition of 1.5 equivalents of sodium borohydride and methanol yielded the corresponding *syn*-3,5-dihydroxyesters (*S*,*R*,*S*)-**11** in good chemical yields (Table V).

Determination of the Relative Configuration

The final confirmation of the relative configuration was conducted *via* two alternative procedures.

On the one hand δ-hydroxy-β-ketoester (*R*,*S*)-**10d** (de = 33% and de ≥ 96%) was cyclised to afford (*S*,*R*)-**14d** followed by selective *O*-methylation to yield 4-methoxy-5,6-dihydropyran-2-one (*S*,*R*)-**15d** (Scheme 4)



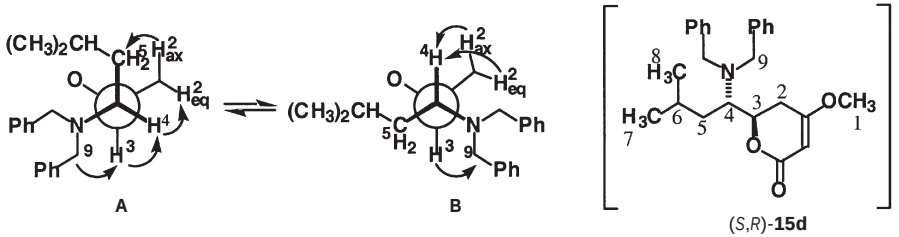
(*R*,*S*)-**10d** (*S*,*R*)-**14d** (*S*,*R*)-**15d**

SCHEME 4

Scheme 5 illustrates the Newman projections along the CH(O)–CH(N) bond of both diastereomers of **15d** and summarises the observed ^{1}H-^{1}H coupling constants as well as the observed NOEs of the ^{1}H NMR spectrum.

The more abundant diastereomer (*S*,*R*)-**15d** is characterised by a small $J_{3,4}$ coupling constant of 5.2 Hz as well as a relatively small NOE between H^3 and H^4 (7%). These findings indicate an equilibrum of *gauche*-conformer **A** and *anti*-conformer **B**, which is further manifested by a strong NOE between H^4 and $H^2{}_{eq}$ as well as between H^4 and $H^2{}_{ax}$. The less abundant diastereomer exhibits a similar ^3J coupling constant of 4.1 Hz, but it clearly differs from the former isomer by a strong NOE (15%) between H^3 and H^4, as well as a small effect between H^4 and $H^2{}_{eq}$ and no detectable effect between H^4 and $H^2{}_{ax}$. Consequently, it emerges that the relative stereochemistry of the more abundant stereoisomer is *anti*.

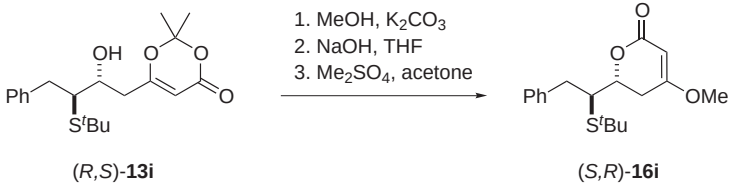
major isomer (*anti*): $J_{3,4}$ = 5.2 Hz



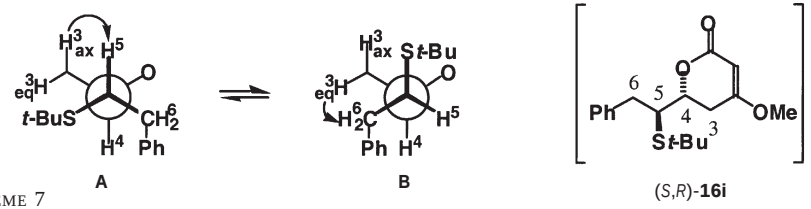
minor isomer (*syn*): $J_{3,4}$ = 4.1 Hz

SCHEME 5

To apply a similar argument for 1,3-dioxin-4-one (*R*,*S*)-**13i**, it was converted into 4-methoxydihydropyran-2-one (*S*,*R*)-**16i** according to Scheme 6. The ^{1}H NMR spectra as well as NOE difference spectra can be explained using the Newman projections in Scheme 7.



SCHEME 6



SCHEME 7

Most notably, the small ^3J coupling constant between H^4 and H^5 (6.5 Hz) as well as the fact that no substantial NOE between them could be detected, leads to the conclusion that both conformers (*anti*-**A** and *gauche*-**B**) in Scheme 7 have to be considered. Further evidence for *anti*-**A** is the fact that

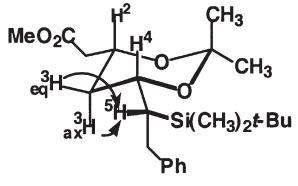
only H^5 exhibits a relatively small effect to H^3_{ax} but no detectable NOE to H^3_{eq}. Finally *gauche*-**B** explains the NOE of H^6 and H^3_{eq}, whereas no effect can be detected between H^6 and H^3_{ax}.

Furthermore, acetalisation of the *syn*-dihydroxyesters (*S*,*R*,*S*)-**11** using 2,2-dimethoxypropane and $BF_3 \cdot OEt_2$ in CH_2Cl_2 yielded the corresponding 1,3-dioxanes (*S*,*S*,*R*)-**17**, of which the relevant ^{13}C NMR resonances are shown in Table VI.

TABLE VI
Yields and ^{13}C NMR resonences of the corresponding 1,3-dioxanes (*S*,*S*,*R*)-**17**

1,3-Dioxane	Yield, %	C-1(δ, ppm)	C-2(δ, ppm)	C-3(δ, ppm)
(*S*,*S*,*R*)-**17a**	55	66.49	19.21	30.03
(*S*,*S*,*R*)-**17b**	68	67.80	19.12	30.08
(*S*,*S*,*R*)-**17c**	81	66.26	19.67	30.02
(*S*,*S*,*R*)-**17e**	90	66.21	19.68	29.99
(*S*,*S*,*R*)-**17f**	90	66.17	19.61	29.99
(*S*,*S*,*R*)-**17l**	83	66.24	19.73	29.96
(*S*,*S*,*R*)-**17j**	67	66.24	19.66	29.81

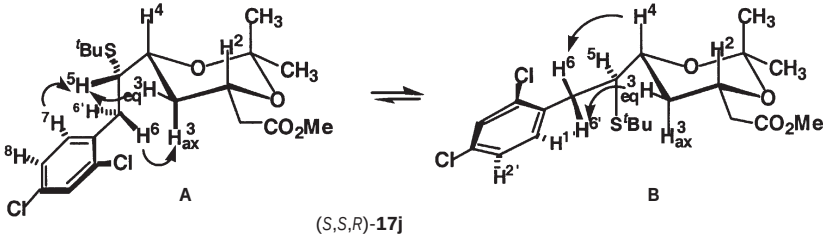
Scheme 8 illustrates the ^1H NMR data ($^3J_{4,5}$ = 2.7 Hz) as well as the observed NOEs of 1,3-dioxane (*S*,*S*,*R*)-**17e**. Most notable is the relatively strong NOE between H^4 and H^5 (14%) as well as the smaller ones between H^5 and H^3_{eq} (3%) and between H^5 and H^3_{ax} (6%). These findings clearly prove the *gauche* orientation of H^4 and H^3 as well as the (*S*,*S*,*R*) configuration as shown.



SCHEME 8 (*S*,*S*,*R*)-**17e**

A similar argument concerning 1,3-dioxane (S,S,R)-**17j** leads to a discussion of both *gauche*-conformers **A** and **B** ($^3J_{4,5}$ = 5.4 Hz; substantial NOE between H^4 and H^5) shown in Scheme 9. Conformer **A** accounts for the small NOE between H^6 and H^5 as well as H^6 and H^3_{ax} and explains the absence of

any detectable effect between H^3_{ax} and $H^{6'}$. Furthermore, the strong effect between H^7 and $H^{6'}$ and the lack of a measurable effect between H^7 and H^6 as well as the substantially stronger NOEs of H^5 to H^3_{eq} as compared to H^3_{ax} is clearly explained by conformer *gauche*-**A**.



SCHEME 9

On the other hand involvement of conformer **B** accounts for the small effect between H^4 and H^6 as well as H^4 and $H^{6'}$. Finally, there is only a small effect between $H^{6'}$ and H^3_{eq} and no measurable effect of $H^{6'}$ and H^3_{ax}.

In summary, these findings again account for the (*S*,*S*,*R*) configuration.

Conclusions

In the present study we unequivocally proved the following points: First, α-heterosubstituted aldehydes, generated efficiently by the SAMP methodology, can be effectively employed in Mukaiyama aldol additions resulting in excellent *anti*-selectivities and good chemical yields. Second, the generated *syn*-dihydroxyesters are a new entry into a novel class of HMGR inhibitors being accessible in two steps in diastereo- and enantiopure form.

EXPERIMENTAL

All reactions were carried out using standard Schlenk techniques unless otherwise stated. Solvents were dried and purified by conventional methods prior to use. Tetrahydrofuran and diethyl ether were freshly distilled from potassium, dichloromethane from CaH_2 under argon. Light petroleum refers to the fraction with a boiling range of 40–80 °C. Reagents of commercial quality were used from freshly opened containers unless otherwise stated.

Enaminoester **4** was prepared following the precedent of Chan *et al.*[20] The chiral pyrrolidine based amines and hydrazines as well as the corresponding hydrazones and enamines were prepared according to known literature precedents[13b,13i,13j]. The various tartarate-based taddolate ligands and the chiral titanium complexes could be obtained according to Seebach *et al.*[19c] Dienes **8** and **12** were prepared following either the two-step silylation methodology[21] and following the protocol of Grunwel *et al.*[29], respectively. Following the precedent of Reetz *et al.*[22f,22i], we prepared α-(dibenzylamino)aldehydes (*S*)-**9a**–(*S*)-9c. The α-silylated and α-sulfenylated aldehydes (*S*)-**9e**–(S)-**9l** were prepared as recently described[23a,24b].

Analytical TLC: Merck glass-backed silica gel 60 F_{254} plates. Preparative column chromatography: Merck silica gel 60, particle size 0.040–0.063 mm (230–400 mesh) (flash). Analytical GC: Siemens Sichromat 2 or 3 equipped with a SE-54-CB column (25 m × 0.25 mm), carrier gas nitrogen, FID. Optical rotations: Perkin–Elmer P 241 polarimeter; solvents of Merck UVASOL quality unless otherwise stated. Specific rotations are given in deg cm^3 g^{-1} dm^{-1}. IR spectra (ν, cm^{-1}): Perkin–Elmer 1420 and Perkin–Elmer FT/IR 1750. ^1H (300 MHz) and ^{13}C NMR spectra (75 MHz) (δ, ppm; *J*, Hz): Varian VXR 300 and Gemini 300 (solvent: $CDCl_3$, TMS as internal standard). Mass spectra: Varian MAT 212 (EI 70 eV) (relative intensities in parentheses). HRMS: Finnigan MAT 95. Microanalyses: Heraeus CHN-O-Rapid.

General Procedure for Aldol Reaction of Chiral Methyl β-Hydrazonobutanoates **1a** (Procedure I)

A flame-dried Schlenk flask was purged with nitrogen and charged with 2.5 equiv. of 2,2,6,6-tetramethylpiperidine in THF (4 ml/mmol). After the addition of 2.5 equiv. of BuLi at 0 °C while stirring, a golden-yellow solution of LTMP was obtained within 10 min and the solution was cooled to –78 °C. The β-hydrazonobutanoate **1a** was added dropwise and the cool bath removed to warm up the solution to 0 °C. Stirring was continued for another 2 h, while a deep orange solution was obtained. After cooling down to –95 °C, an aldehyde was added slowly dropwise and the reaction mixture was warmed up overnight. The reaction was quenched by addition of glacial acetic acid (0.37 ml/mmol). Extractive work-up with diethyl ether/water (100 ml/10 ml) yielded the crude γ-hydrazonopyrans which were dissolved in diethyl ether (20 ml/mmol). 1.4 M HCl (1 ml/mmol) was added and the resulting two-phase system was stirred at room temperature for another 15 h to cleave off the chiral auxiliary. Separation of the organic phase and standard extractive work-up with diethyl ether yielded the crude γ-ketopyrans **2**, which were finally purified by column chromatography.

General Procedure for Aldol Reaction of Chiral β-Enaminobutanoates **1b** (Procedure II)

A flame-dried Schlenk flask was purged with nitrogen and charged with 2.0 equiv. diisopropylamine in THF (4 ml/mmol). After dropwise addition of 2.0 equiv. of BuLi at 0 °C with stirring a light-yellow solution of LDA was obtained within 10 min. The solution was cooled to –78 °C and 2.0 equiv. of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine were added dropwise followed by the corresponding β-enaminobutanoate **1b**. Stirring was continued for another hour at that temperature yielding a yellow solution of the corresponding enolate. After cooling to –95 °C the aldehyde was added slowly dropwise and the reaction mixture was stirred for another hour while warming up to –78 °C. The reaction was quenched by adding glacial acetic acid (0.37 ml/mmol) and standard extractive work-up with diethyl ether (30 ml/mmol) and water (3 ml/mmol) yielded the crude β-enaminoester which was dissolved in diethyl ether (20 ml/mmol). 1.4 M HCl (1 ml/mmol) was added and the resulting two-phase system was stirred at room temperature for another 15 h to cleave the chiral auxiliary. Separation of the organic phase followed by standard extraction work-up with diethyl ether yielded the crude δ-hydroxy-β-ketoesters **3**, which were finally purified by column chromatography.

General Procedure for Aldol Reaction of Enaminoester **4** Using Chiral Titanium Complexes (Procedure III)

A flame-dried Schlenk flask was purged with nitrogen and charged with 1.1 equiv. of diisopropylamine in THF (4 ml/mmol). At 0 °C 1.1 equiv. of BuLi were added while stirring to yield a light-yellow solution of LDA within 10 min. The solution was cooled to –78 °C and the β-enaminobutanoate **4** was slowly added. Stirring was continued for another hour at that temperature yielding a yellow solution of the corresponding enolate. The corresponding titanium complex (0.5 M solution in THF) was added at the same temperature, resulting in a dark orange solution. After stirring for another hour at the same temperature the aldehyde was added slowly and the reaction mixture was allowed to warm up to room temperature overnight. The reaction was quenched by adding 20% neutral aqueous KF solution (1.0 ml/mmol) and standard extraction work-up with diethyl ether (30 ml/mmol) and water (10 ml/mmol) yielded the crude β-enaminoester **5** which was finally purified by column chromatography.

General Procedure for $TiCl_4$-Mediated Addition of 1-Methoxy-1,3-bis[(trimethylsilyl)oxy]-butadiene **8** to Achiral Aldehydes Using Chiral Titanium Catalysts (Procedure IV)

A flame-dried Schlenk flask was charged with a solution of the corresponding achiral aldehyde in dichloromethane (10 ml/mmol) and cooled to –78 °C. After the dropwise addition of the corresponding titanium complex (0.5 M solution in DCM) the resulting complex precipitated, yielding a light yellow heterogenous mixture. Two equivalents of 1-methoxy-1,3-bis[(trimethylsilyl)oxy]butadiene **8** dissolved in dichloromethane (1 ml/mmol) were added and stirring was continued at the same temperature for another 2 h. The resulting reaction mixture was quenched by adding dry methanol (1 ml/mmol) and poured into a separating funnel. After addition of diethyl ether (50 ml/mmol) and pH-7 buffer (10 ml/mmol) the organic layer was separated and standard aqueous work-up followed by purification using column chromatography afforded pure δ-hydroxy-β-ketoesters **3** as colourless oils.

General Procedure for $TiCl_4$-Mediated Addition of 1-Methoxy-1,3-bis[(trimethylsilyl)oxy]-butadiene **8** to Enantiomerically Enriched Aldehydes **9** (Procedure V)

A flame-dried Schlenk flask was charged with a solution of 1-methoxy-1,3-bis[(trimethylsilyl)oxy]butadiene **8** (2.34 g, 9.0 mmol) in dichloromethane (30 ml) and cooled to –78 °C. After simultaneous dropwise addition of the corresponding α-heterosubstituted aldehyde **9** (3.0 mmol in 12.4 ml dichloromethane) and titanium tetrachloride solution (12.4 ml, c = 0.5 mol/l in dichloromethane, 6.2 mmol) *via* motorized syringe pumps, the dark reaction mixture was stirred for further 30 min followed by addition of methanol (3 ml). The orange mixture was poured into a separating funnel followed by diethyl ether (300 ml) and pH-7 buffer (50 ml) and the organic layer was separated. The aqueous layer was extracted twice with diethyl ether (50 ml) and the combined organic phase was washed with brine, dried over magnesium sulfate and filtered. Evaporation of the solvent *in vacuo* and purification by column chromatography afforded pure hydroxyesters (*R*,*S*)-**10** as colourless oils.

General Procedure for BF_3 Etherate-Mediated Addition of 2,2-Dimethyl-4-methylidene-6-[(trimethylsilyl)oxy]-1,3-dioxine **12** to α-Alkyl- or α-Arylsulfanylaldehydes (*S*)-**9i** and (*S*)-**9l** (Procedure VI)

A flame-dried Schlenk flask was charged with a solution of the (*S*)-**9i** or (*S*)-**9l** (2 mmol) in dichloromethane (10 ml) and cooled to –78 °C. After dropwise addition of boron trifluoride etherate (0.62 ml, 4.2 mmol) and further stirring for 10 min a solution of 2,2-dimethyl-4-methylidene-6-[(trimethylsilyl)oxy]-1,3-dioxine **12** (1.07 g, 5 mmol in 5 ml of dichloromethane) was added dropwise. After stirring for a further 1 h the orange solution was poured into a separating funnel followed by diethyl ether (50 ml) and pH-7 buffer (10 ml) and the organic layer was separated. The aqueous layer was extracted twice with diethyl ether (50 ml) and the combined organic phase was washed with brine, dried over magnesium sulfate and filtered. Evaporation of the solvent *in vacuo* and purification by column chromatography afforded pure hydroxylactones (*R*,*S*)-**13** as colourless oils.

General Procedure for *syn*-Reduction of δ-Hydroxy-β-ketoesters **10** (Procedure VII)

A flame-dried Schlenk flask was charged with a solution of tributylborane (1.1 equiv.) in THF (10 ml/mmol) and a δ-hydroxy-β-ketoester **10** was added dropwise as a solution in THF (c = 0.1 mol/l) at room temperature. After the addition of pivalic acid (0.01 equiv.) stirring was continued for another 15 min and the reaction mixture was subsequently cooled to –95 °C. Sodium borohydride (1.5 equiv.) was added in one portion followed by the dropwise addition of dry methanol (0.8 ml/mmol). After warming up to room temperature overnight the reaction was quenched by addition of glacial acetic acid (1 ml/mmol) followed by a standard aqueous work-up with diethyl ether. The resulting crude boronate was saponified by three-fold azeotropic distillation using methanol (10 ml/mmol). The resulting sirup was finally purified by column chromatography to afford diols (*S*,*R*,*S*)-**11** as colourless oils.

General Procedure for Lactonisation and Methylation of δ-Hydroxy-β-ketoesters **10** (Procedure VIII)

A round bottomed flask was charged with a solution of a hydroxyester **10** in THF (5 ml/mmol) and 1 M NaOH (1 equiv.) was added dropwise while cooling in an ice bath. After warming up to room temperature stirring was continued for another 45 min and the reaction mixture was subsequently acidified with 1 M aqueous hydrochloric acid. Standard aqueous work-up with diethyl ether (30 ml/mmol) and water (3 ml/mmol) resulted in a sirup, which was finally purified by column chromatography, and the resulting β-ketopyranone was dissolved in acetone (5 ml/mmol) using a round bottomed flask. Dry potassium carbonate (2 equiv.) was added followed by dimethyl sulfate (1.1 equiv.) and stirred at room temperature for another 12 h. The reaction was quenched by adding water (5 ml/mmol) and standard extractive work-up with diethyl ether (30 ml/mmol) yielded the crude 4-methoxy-5,6-dihydropyran-2-one **15**, which was finally purified by column chromatography.

General Procedure for Acetalisation of *syn*-1,3-Dihydroxyesters (*S*,*R*,*S*)-**11** (Procedure IX)

An oven-dried round bottom flask was charged with 2,2-dimethoxypropane (10 equiv.) in CH_2Cl_2 (5 ml/mmol) and was cooled to –78 °C. After the slow addition of boron trifluoride etherate (10 equiv.). Stirring was continued for another 10 min and the corresponding diol

(*S*,*R*,*S*)-**11** was added in CH_2Cl_2 (1 ml/mmol). The reaction mixture was allowed to warm to room temperature over 6 h and the resulting red solution was poured into a separation funnel followed by diethyl ether (100 ml/mmol) and water (10 ml/mmol). The organic phase was separated and washed with saturated aqueous sodium hydrogencarbonate solution and brine and dried over magnesium sulfate. After filtering off the drying agent and removing the solvent under reduced pressure the remaining sirup was purified by column chromatography to yield the 1,3-dioxanes (*S*,*S*,*R*)-**17** as sirups or solids.

(*S*)-(–)-*2-(tert-Butyldimethylsilyl)-3-(2,4-dichlorophenyl)propanal*[24b] ((*S*)-**9e**): 2.5 g (72%) yield from (*S*)-(+)-1-{[2-(*tert*-butyldimethylsilyl)ethylidene]amino}-2-(methoxymethyl)pyrrolidine after column chromatography (silica gel, light petroleum/diethyl ether, 4:1); R_F 0.78 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ –52.6 (*c* 1.03, C_6H_6); ee = 92%, determined after reduction and esterification with (*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoic acid by ^{1}H NMR. IR (film): 3380, 3082, 3060, 2945, 2922, 2878, 2852, 2817, 2719, 1925, 1895, 1695 (CO), 1585, 1467, 1440, 1419, 1385, 1362, 1338, 1300, 1280, 1250, 1180, 1099, 1068, 1048, 1007, 947, 863, 850, 830, 819, 770, 703, 689, 669, 658. ^{1}H NMR: 0.14 s, 3 H (H-10); 0.21 s, 3 H (H-10′); 1.00 s, 9 H (H-12); 2.87 dd, 1 H, *J*(3,3′) = 14.0, *J*(3,2) = 2.2 (H-3); 3.00 ddd, 1 H, *J*(2,3′) = 11.5, *J*(2,1) = 2.5, *J*(2,3) = 2.2 (H-2); 3.31 dd, 1 H, *J*(3′,3) = 14.0, *J*(3′,2) = 11.5 (H-3′); 7.12 dd, 1 H, *J*(8,9) = 8.2, *J*(8,6) = 1.9 (H-8); 7.25 d, 1 H, *J*(9,8) = 8.2 (H-9); 7.31 d, 1 H, *J*(6,8) = 1.9 (H-6); 9.64 d, 1 H, *J*(1,2) = 2.5. ^{13}C NMR: –6.51 (C-10), –6.21 (C-10′), 17.90 (C-11), 26.88 (C-12), 28.20 (C-3), 47.98 (C-2), 126.92 (C-8), 129.13 (C-9), 132.31 (C-6), 132.51 (C-7), 133.94 (C-5), 137.88 (C-4), 201.40 (C-1). MS (70 eV, *m*/*z* (rel.%)): 316 (1.1) [M^+], 301 (3.5) [$M^+ - CH_3$], 259 (100) [$M^+ - C_4H_9$], 247 (1.6), 231 (1.8), 223 (3.7), 203 (63), 185 (17.1), 167 (13.7), 159 (9.7) [$C_7H_5Cl_2^+$], 149 (9.4), 131 (6.8), 115 (9.8) [TBDMS$^+$], 105 (13.9), 95 (26.7), 93 (75.3), 75 (50.6) [$C_2H_7SiO^+$], 73 (67), 59 (27.8), 45 (10) [$C_3H_7^+$], 43 (8), 41 (7). For $C_{15}H_{22}Cl_2OSi$ (316.1) calculated: 56.77% C, 6.99% H; found: 56.39% C, 7.01% H.

(S)-(–)-2-(tert-Butylsulfanyl)-3-(2,4-dichlorophenyl)propanal[23a] ((*S*)-**9j**): 1.8 g (54%) yield from (*S*)-(+)-1-{[2-(*tert*-butylsulfanyl)ethylidene]amino}-2-(methoxymethyl)pyrrolidine after column chromatography (silica gel, light petroleum/diethyl ether, 4:1); R_F 0.55 (light petroleum/diethyl ether, 10:1); $[\alpha]_D^{20}$ –142.0 (*c* 1.7, C_6H_6); ee = 94%, determined after reduction and esterification with (*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoic acid by ^{1}H NMR. IR (film): 3402, 3091, 3075, 3035, 2967, 2927, 2862, 2838, 2726, 1709 (CO), 1589, 1562, 1475, 1459, 1436, 1389, 1380, 1367, 1339, 1293, 1256, 1218, 1205, 1172, 1153, 1102, 1073, 1050, 988, 958, 934, 868, 817, 762, 717, 679, 656, 621, 584, 563. ^{1}H NMR: 0.75 s, 9 H (H-11); 2.71 dd, 1 H, *J*(3,3′) = 14.0, *J*(3,2) = 7.7 (H-3); 3.08 dd, 1 H, *J*(3′,3) = 14.0, *J*(3′,2) = 7.7 (H-3′); 3.38 td, 1 H, *J*(2,3′) = *J*(2,3) = 7.7, *J*(2,1) = 3.0 (H-2); 6.74 d, 1 H, *J*(9,8) = 8.2 (H-9); 6.80 dd, 1 H, *J*(8,9) = 8.2, *J*(8,6) = 2.0 (H-8); 7.12 d, 1 H, *J*(6,8) = 2.0 (H-6); 9.24 d, 1 H, *J*(1,2) = 3.0. ^{13}C NMR: 30.83 (C-11), 33.04 (C-3), 44.39 (C-10), 50.75 (C-2), 127.00 (C-8), 129.32 (C-9), 133.47 (C-7), 133.76 (C-6), 134.54 (C-5), 134.98 (C-4), 193.24 (C-1). MS (70 eV, *m*/*z* (rel.%)): 290 (0.4) [M^+], 261 (1.6) [$M^+ - C_4H_8$], 255 (7.9), 199 (7.5), 169 (3.1), 159 (8.4), 134 (2.8), 102 (3.4), 89 (4.7), 57 (100) [$C_4H_9^+$], 41 (25.3). For $C_{13}H_{16}Cl_2OS$ (291.2) calculated: 53.61% C, 5.54% H; found: 53.80% C, 5.62% H.

(S)-(–)-2-(Phenylsulfanyl)-3-methylbutanal[23a] ((*S*)-**9l**): 2.3 g (60%) yield from (*S*)-(+)-1-{[2-(phenylsulfanyl)ethylidene]amino}-2-(methoxymethyl)pyrrolidine after column chromatography (silica gel, light petroleum/diethyl ether, 4:1); R_F 0.69 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ –26.0 (*c* 0.95, C_6H_6); ee = 84%, determined after reduction and esterification with (*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoic acid by ^{1}H NMR. IR (film): 3413, 3059, 3010, 2963, 2932, 2872, 2812, 2715, 1953, 1879, 1800, 1718 (CO), 1584, 1482, 1467, 1439,

1389, 1370, 1340, 1325, 1252, 1189, 1166, 1135, 1089, 1068, 1049, 1025, 1001, 986, 930, 898, 741, 691. ^{1}H NMR: 1.07 d, 3 H, *J*(4,3) = 6.9 (H-4); 1.18 d, 3 H, *J*(4,3) = 6.6 (H-4′); 2.09 dqq, 1 H, *J*(3,2) = 8.5, *J*(3,4) = 6.9, *J*(3,4′) = 6.6 (H-3); 3.27 dd, 1 H, *J*(2,3) = 8.5, *J*(2,1) = 5.3 (H-2); 7.20–7.40 m, 5 H (H-6, H-7 and H-8); 9.35 d, 1 H, *J*(1,2) = 5.3. ^{13}C NMR: 19.99 (C-4), 20.68 (C-4′), 27.85 (C-3), 64.46 (C-2), 127.78 (C-7), 129.14 (C-6), 132.20 (C-8), 132.68 (C-5), 194.96 (C-1). MS (70 eV, *m/z* (rel.%)): 194 (48.9) [M^+], 165 (100) [M^+ – CHO], 137 (3.5), 123 (54.5), 109 (18.9), 91 (4.1) [$C_7H_7^+$], 87 (8.8), 77 (5.5), 55 (46.4), 45 (19.7), 41 (12.5), 39 (15.7). For $C_{11}H_{14}OS$ (194.3) calculated: 68.00% C, 7.26% H; found: 68.17% C, 7.28% H.

Methyl (5R,6S)-(+)-6-(dibenzylamino)-5-hydroxy-7-methyl-3-oxooctanoate ((*R,S*)-**10a**): 0.85 g (60%) yield from aldehyde **9a** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1); R_F 0.36 (light petroleum/diethyl ether, 2:1) following procedure V; $[\alpha]_D^{20}$ 3.0 (*c* 1.0, CH_2Cl_2); de = 97%, determined by NMR; ee > 96%, determined after *syn*-reduction and acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3085, 3062, 3028, 2954, 2836, 2803, 2718, 2208, 1950, 1879, 1747, 1713 ($COOCH_3$), 1654, 1631, 1602, 1568, 1494, 1453, 1438, 1404, 1385, 1362, 1323, 1245, 1208, 1154, 1100, 1070, 1029, 1014, 973, 913, 865, 846, 750, 700. ^{1}H NMR: 1.04 d, 3 H, *J*(7,8) = 6.6 (H-8); 1.15 d, 3 H, *J*(7,8′) = 6.6 (H-8′); 2.20 dsept, 1 H, *J*(6,7) = 6.9, *J*(7,8) = 6.6 (H-7); 2.44 dd, 1 H, *J*(6,7) = 6.6, *J*(6,5) = 6.3 (H-6); 2.58 dd, 1 H, *J*(4,5) = 10.4, *J*(4,4′) = 16.8 (H-4); 2.90 dd, 1 H, *J*(4,4′) = 16.8, *J*(4′,5) = 1.9 (H-4′); 3.44 d, 1 H, *J*(2,2′) = 15.7 (H-2); 3.49 d, 1 H, *J*(2,2′) = 15.7 (H-2′); 3.66 d, 2 H, *J*(9,9′) = 13.4 (H-9); 3.70 s, 3 H (OCH_3); 3.75 d, 2 H, *J*(9,9′) = 13.4 (H-9′); 4.30 m, 1 H, (H-5); 7.21–7.36 m, 10 H (H-11, H-12, H-13). ^{13}C NMR: 20.02 (C-8), 23.45 (C-8′), 26.65 (C-7), 47.78 (C-4), 49.75 (C-2), 52.35 (OCH_3), 55.37 (C-9), 65.53 (C-6), 66.47 (C-5), 127.19 (C-12), 128.43 (C-11), 129.06 (C-13), 139.60 (C-10), 167.48 (C-1), 203.73 (C-3). MS (70 eV, *m/z* (rel.%)): 397 (0.7) [M^+], 366 (2) [M^+ – OCH_3], 354 (6) [M^+ – C_3H_7], 336 (4) [M^+ – H_2O – C_3H_7], 252 (100) [$C_{19}H_{23}NO^+$ – CHO], 181 (9), 91 (89) [$C_7H_7^+$], 65 (5), 43 (4). HRMS $C_{21}H_{24}NO_4$](M^+ – C_3H_7) calculated: 354.1705; found: 354.1708.

Methyl (5R,6S)-(–)-6-(dibenzylamino)-5-hydroxy-7,7-dimethyl-3-oxooctanoate ((*R,S*)-**10b**): 1.05 g (71%) yield from aldehyde **9b** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure V; R_F 0.35 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ –25.4 (*c* 1.1, CH_2Cl_2); de > 96%, determined by NMR; ee > 96%, determined after *syn*-reduction and acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3085, 3063, 3025, 2954, 2911, 2872, 2801, 1950, 1745, 1712 (COOMe), 1654, 1602, 1494, 1453, 1438, 1402, 1359, 1325, 1217, 1154, 1122, 1073, 1028, 962, 918, 852, 757, 701, 668. ^{1}H NMR: 1.08 s, 9 H (H-8); 2.38 d, 1 H, *J*(5,6) = 4.1 (H-6); 2.76 dd, 1 H, *J*(4,4′) = 17.9, *J*(4,5) 8.5 (H-4); 2.83 dd, 1 H, *J*(4′,4) 17.9, *J*(4′,5) = 8.2 (H-4′); 3.36 d, 1 H, *J*(2,2′) = 16.7 (H-2); 3.40 d, 1 H, *J*(2,2′) = 16.7 (H-2′); 3.62–3.73 d br, 2 H, *J*(9,9′) = 13.7 (H-9); 3.75 s, 3 H (OCH_3); 3.92–4.13 m br, 2 H (H-9′); 4.49 ddd, 1 H, *J*(5,4) = 8.5, *J*(5,4′) = 8.2, *J*(5,6) = 4.1 (H-5); 7.20–7.36 m, 10 H (H-11, H-12, H-13). ^{13}C NMR: 29.84 (C-8), 37.63 (C-7), 49.46 (C-4), 50.59 (C-2), 52.44 (OCH_3), 56.41 (br, C-9), 67.42 (C-6), 67.48 (C-5), 126.94 (C-12), 128.22 (C-11), 129.35 (br, C-13), 140.05 (br, C-10), 167.3 (C-1), 204.15 (C-3). MS (70 eV, *m/z* (rel.%)): 411 (0.2) [M^+], 380 (1) [M^+ – OCH_3], 354 (23) [M^+ – C_4H_9], 336 (2) [M^+ – H_2O – C_4H_9], 322 (4) [354$^+$ – CH_3OH], 266 (33) [$C_{20}H_{25}NO^+$ – CHO], 181 (9), 91 (100) [$C_7H_7^+$], 65 (9), 43 (25) [$C_3H_7^+$]. HRMS $C_{21}H_{24}NO_4$ (M^+ – C_4H_9) calculated: 354.1705; found: 354.1706.

Methyl (5R,6S)-(+)-6-(dibenzylamino)-5-hydroxy-3-oxo-7-phenylheptanoate ((*R,S*)-**10c**): 0.94 g (67%) yield from aldehyde **9d** after column chromatography (silica gel, light petroleum/di-

ethyl ether, 4:1) following procedure V; R_F 0.32 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ +16.2 (*c* 1.5, CH_2Cl_2); de = 97%, determined by NMR; ee > 96%, determined after *syn*-reduction and acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3650–3200, 3084, 3061, 3027, 2953, 2929, 2850, 2804, 1950, 1875, 1810, 1747, 1713 (COOMe), 1654, 1630, 1602, 1494, 1454, 1438, 1404, 1373, 1323, 1249, 1207, 1153, 1121, 1074, 1028, 1020, 974, 909, 858, 746, 700. ^{1}H NMR: 2.44 dd, 1 H, *J*(7,7′) = 17.6, *J*(7,6) = 9.9 (H-7); 2.80 s br, 1 H (OH); 2.93 m, 1 H (H-6); 2.97 dd, 1 H, *J*(7,7′) = 17.6, *J*(7′,6) = 1.9 (H-7′); 2.99 dd, 1 H, *J*(4,4′) = 14.1, *J*(4,5) = 5.7 (H-4); 3.08 dd, 1 H, *J*(4,4′) = 14.1, *J*(4′,5) = 7.4 (H-4′); 3.34 d, 1 H, *J*(2,2′) = 15.7 (H-2); 3.39 d, 1 H, *J*(2,2′) = 15.7 (H-2′); 3.58 d br, 2 H, *J*(12,12′) = 13.7 (H-12); 3.70 s, 3 H (OCH_3); 3.73 d br, 2 H, *J*(12,12′) = 13.7 (H-12′); 4.28 m, 1 H (H-5); 7.13–7.34 m, 15 H (H-9, H-10, H-11, H-14, H-15, H-16). ^{13}C NMR: 32.29 (C-7), 47.95 (C-4), 49.58 (C-2), 52.39 (OCH_3), 54.65 (C-12), 62.92 (C-6), 68.46 (C-5), 125.96 (C-10), 126.99 (C-15), 128.26 (C-9), 128.37 (C-14), 128.83 (C-11), 129.41 (C-16), 139.38 (C-8), 141.00 (C-13), 167.33 (C-1), 203.92 (C-3). MS (70 eV, *m/z* (rel.%)): 445 (0.1) [M^+], 354 (14) [$M^+ - C_3H_7$], 336 (2) [354 – H_2O], 322 (3) [354 – CH_3OH], 300 (66) [$C_{22}H_{22}N^+$], 181 (6), 132 (2), 92 (8), 91 (100) [$C_7H_7^+$], 65 (5), 44 (4.0). For $C_{28}H_{31}NO_4$ (445.6) calculated: 75.48% C, 7.01% H, 3.14% N; found: 75.38% C, 7.33% H, 3.57% N.

Methyl (5R,6S)-(–)-6-(dibenzylamino)-5-hydroxy-8-methyl-3-oxononanoate ((*R,S*)-**10d**): 0.86 g (70%) yield from aldehyde **9d** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure V; R_F 0.32 (light petroleum/diethyl ether, 1:2); $[\alpha]_D^{20}$ –1.8 (*c* 1.1, CH_2Cl_2); de = 95%, determined by NMR; ee > 96%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3086, 3062, 3029, 2953, 2866, 2841, 2804, 1955, 1855, 1747 (COOMe), 1713 (COOMe), 1654, 1603, 1513, 1494, 1453, 1438, 1405, 1384, 1367, 1322, 1245, 1217, 1209, 1157, 1105, 1068, 1028, 966, 918, 849, 749, 700, 681. ^{1}H NMR: 0.77 d, 3 H, *J*(9,8) = 6.3 (H-9); 0.92 d, 3 H, *J*(9′,8) = 6.6 (H-9′), 1.28 ddd, 1 H, *J*(7,7′) = 14.0, *J*(7,6) = 6.9, *J*(7,8) = 6.5, 1 H (H-7); 1.65 ddd, 1 H, *J*(7,7′) = 14.0, *J*(7′,8) = 6.9, *J*(7′,6) = 6.5, 1 H (H-7′); 1.86 m, 1 H (H-8); 2.55 dd, 1 H, *J*(4,4′) = 17.0, *J*(4,5) = 9.6, 1 H (H-4); 2.58 ddd, 1 H, *J*(7,6) = 6.5, *J*(7′,6) = 6.3, *J*(6,5) = 5.5 (H-6); 2.82 dd, 1 H, *J*(4,4′) = 17.0, *J*(4′,5) = 2.2 (H-4′); 2.90 m br, 1 H (OH); 3.40 d, 1 H, *J*(2,2′) = 15.6 (H-2); 3.45 d, 1 H, *J*(2,2′) = 15.6, 1 H (H-2′); 3.62 d br, 2 H, *J*(10,10′) = 14.0 (H-10); 3.66 d br, 2 H, *J*(10,10′) = 14.0 (H-10′); 3.73 s, 3 H (OCH_3); 4.25 m, 1 H (H-5); 7.22–7.32 m, 10 H (H-12, H-13, H-14). ^{13}C NMR: 22.78 (C-9), 23.17 (C-9′), 25.26 (C-8), 35.43 (C-7), 47.87 (C-4), 49.67 (C-2), 52.39 (OCH_3), 54.71 (br, C-10), 58.36 (C-6), 67.70 (C-5), 127.02 (C-13), 128.30 (C-12), 129.00 (C-14), 140.00 (C-11), 167.40 (C-1), 203.86 (C-3). MS (70 eV, *m/z* (rel.%)): 411 (0.1) [M^+], 380 (1) [$M^+ - OCH_3$], 354 (1) [$M^+ - C_4H_9$], 266 (100) [$C_{19}H_{24}N^+$], 181 (8), 91 (11) [$C_7H_7^+$], 65 (3), 42 (3). HRMS $C_{24}H_{30}NO_3$ ($M^+ - OCH_3$) calculated: 380.22257; found: 380.22247.

Methyl (5R,6S)-(+)-6-(tert-butyldimethylsilyl)-5-hydroxy-3-oxo-7-phenylheptanoate ((*R,S*)-**10e**): 0.76 g (54%) yield from aldehyde **9e** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure V; R_F 0.27 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ +45.2 (*c* 0.93, CH_2Cl_2); de = 95%, determined by NMR; ee = 93%, determined after *syn*-reduction and acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3100 (OH), 3084, 3062, 3025, 2955, 2929, 2899, 2883, 2856, 1945, 1870, 1746, 1712 (COOMe), 1654, 1631, 1602, 1495, 1471, 1454, 1438, 1404, 1362, 1325, 1253, 1217, 1148, 1108, 1058, 1009, 825, 810, 700. ^{1}H NMR: 0.07 s, 3 H (H-12); 0.12 s, 3 H (H-12′); 0.96 s, 9 H

(H-14); 1.46 ddd, 1 H, *J*(6,7) = 9.1, *J*(6,7′) = 4.4, *J*(6.5) = 2.5 (H-6); 2.31 dd, 1 H, *J*(4,4′) = 17.8, *J*(4,5) = 3.0 (H-4); 2.50 dd, 1 H, *J*(4,4′) = 17.8, *J*(4′,5) = 9.3, 1 H (H-4′); 2.76–2.90 m, 2 H (H-7, H-7′); 3.15 d, 1 H, *J*(2,2′) = 15.6 (H-2); 3.20 d, 1 H, *J*(2,2′) = 15.6 (H-2′); 3.66 s, 3 H (OCH_3); 4.35 ddd, 1 H, *J*(5,4) = 9.3, *J*(5,4′) = 3.0, *J*(4,5) = 2.5 (H-5); 7.14–7.32 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: –5.96 (C-12), –5.81 (C-12′), 17.59 (C-13), 27.29 (C-14), 30.09 (C-6), 31.14 (C-7), 49.38 (C-4), 49.69 (C-2), 52.33 (OCH_3), 68.22 (C-5), 125.83 (C-10), 128.41 (C-9), 128.54 (C-11), 143.90 (C-8), 167.26 (C-3), 204.13 (C-1). MS (70 eV, *m/z* (rel.%)): 364 (0.1) [M^+], 331 (2) [$M^+ - H_2O - CH_3$], 289 (76) [$M^+ - H_2O - C_4H_9$], 275 (4) [$M^+ - CH_3OH - C_4H_9$], 207 (8), 201 (4), 191 (8), 183 (5), 173 (16), 155 (21), 141 (7), 131 (27), 117 (34), 115 (12) [$TBDMS^+$], 107 (6), 101 (9), 91 (49) [$C_7H_7^+$], 75 (100) [$C_2H_7OSi^+$], 73 (43) [TMS^+], 59 (17). For $C_{20}H_{32}O_4Si$ (364.6) calculated: 65.89% C, 8.85% H; found: 65.89% C, 8.60% H.

Methyl (5R,6S)-(+)-6-(tert-butyldimethylsilyl)-7-(2,4-dichlorophenyl)-5-hydroxy-3-oxoheptanoate ((*R,S*)-**10f**): 0.65 g (60%) yield from aldehyde **9f** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1); R_F 0.29 (light petroleum/diethyl ether, 4:1) following procedure V; $[\alpha]_D^{20}$ +47.9 (*c* 0.61, CH_2Cl_2); de = 95%, determined by NMR; ee = 95%, determined after *syn*-reduction and acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3650–3300 (OH), 3060, 3040, 2945, 2925, 2895, 2880, 2855, 1950, 1840, 1745, 1710 (COOMe), 1650, 1630, 1585, 1555, 1468, 1440, 1405, 1385, 1320, 1250, 1200, 1155, 1135, 1100, 1050, 1010, 820, 808, 770. ^{1}H NMR: 0.07 s, 3 H (H-14); 0.13 s, 3 H (H-14′); 0.95 s, 9 H (H-16); 1.54 ddd, 1 H, *J*(6,7) = 11.3, *J*(6,7′) = 3.6, *J*(6,5) = 1.9 (H-6); 2.33 dd, 1 H, *J*(4,4′) = 12.8, *J*(4,5) = 4.1 (H-4); 2.39 dd, 1 H, *J*(4,4′) = 12.8, *J*(4′,5) = 8.2 (H-4′); 2.65–2.80 s br, 1 H (OH); 2.80 dd, 1 H, *J*(7,7′) = 15.1, *J*(7,6) = 3.6 (H-7); 3.03 dd, 1 H, *J*(7,7′) = 15.1, *J*(7′,6) = 11.3 (H-7′); 3.28 s, 2 H (H-2, H-2′); 3.69 s, 3 H (OCH_3); 4.33 ddd, 1 H, *J*(5,4) = 8.2, *J*(5,4′) = 4.1, *J*(6,5) = 1.9 (H-5); 7.18 dd, 1 H, *J*(12,13) = 8.2, *J*(12,10) = 2.2 (H-12); 7.28 d, 1 H, *J*(13,12) = 8.2 (H-13); 7.36 d, 1 H, *J*(12,10) = 2.2 (H-10). ^{13}C NMR: –5.88 (C-14), –5.78 (C-14′), 17.55 (C-15), 27.23 (C-16), 28.82 (C-6), 28.98 (C-7), 49.48 (C-2, C-4), 52.41 (OCH_3), 67.70 (C-5), 127.01 (C-12), 129.39 (C-13), 132.11 (C-10), 132.21 (C-11), 134.52 (C-9), 139.62 (C-8), 167.18 (C-1), 204.09 (C-3). MS (70 eV, *m/z* (rel.%)): 417 (0.2) [$M^+ - CH_3$], 399 (3) [$M^+ - CH_3 - H_2O$], 357 (90) [$M^+ - H_2O - C_4H_9$], 343 (5) [$M^+ - CH_3OH - C_4H_9$], 329 (7), 315 (7), 269 (8), 259 (16), 227 (7), 223 (6), 201 (11), 199 (16), 173 (16), 159 (39) [$C_7H_5Cl_2^+$], 129 (5), 115 (8) [$TBDMS^+$], 101 (12), 93 (17), 89 (31), 75 (100.0) [$C_2H_7SiO^+$], 59 (23), 43 (39) [$C_3H_7^+$]. For $C_{20}H_{30}Cl_2O_4Si$ (433.5) calculated: 55.42% C, 6.97% H; found: 55.40% C, 6.94% H.

Methyl (5R,6S)-(+)-6-(tert-butylsulfanyl)-5-hydroxy-3-oxo-7-phenylheptanoate ((*R,S*)-**10g**): 0.89 g (87%) yield from aldehyde **9g** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure V; R_F 0.44 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ +52.0 (*c* 1.21, CH_2Cl_2); de = 95%, determined by NMR; ee = 93%, determined after *syn*-reduction and acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3085, 3061, 3028, 2958, 2927, 2899, 2863, 1950, 1870, 1718 (COOMe), 1654, 1631, 1604, 1495, 1439, 1406, 1366, 1325, 1262, 1205, 1162, 1115, 1077, 1031, 933, 860, 810, 753. ^{1}H NMR: 1.18 s, 9 H (H-13); 2.76 dd, 1 H, *J*(4,4′) = 16.5, *J*(4,5) = 9.1 (H-4); 2.79–3.01 m, 3 H (H-4′, H-7, H-7′); 3.02 ddd, 1 H, 1 H, *J*(6,7) = 8.2, *J*(6,7′) = 6.3, *J*(6,5) = 4.4 (H-6); 3.48 s, 2 H (H-2, H-2′); 3.73 s, 3 H (OCH_3); 4.17 m, 1 H (H-5); 7.20–7.32 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: 31.37 (C-13), 39.42 (C-7), 43.86 (C-12), 46.45 (C-4), 49.55 (C-2), 50.81 (C-6), 52.39 (OCH_3), 69.23 (C-5), 126.52 (C-10), 128.31 (C-9), 128.56 (C-11), 138.91 (C-8), 167.43 (C-1), 202.22 (C-3). MS (70 eV, *m/z* (rel.%)): 338 (10.0) [M^+], 320 (7.1) [$M^+ - H_2O$], 295 (0.7) [M^+ –

CH_3CO], 264 (2.0), 247 (10.0) [$M^+ - C_7H_7$], 230 (7), 222 (1.5), 193 (16.5), 173 (57.6), 166 (3.2), 159 (7.8), 145 (19.4) [$C_6H_9O_4^+$], 137 (77), 129 (4.1), 117 (6.0), 113 (12), 104 (10), 101 (12.3), 91 (34.7) [$C_7H_7^+$], 85 (3.5), 77 (4.7), 71 (4.7), 57 (100) [$C_4H_9^+$], 43 (21.2) [$C_3H_7^+$], 41 (22.3) [$C_3H_5^+$]. For $C_{18}H_{26}O_4S$ (338.5) calculated: 63.88% C, 7.74% H; found: 64.20% C, 8.01% H.

Methyl (5R,6S)-(+)-6-(tert-butylsulfanyl)-7-(2′,4′-dichlorophenyl)-5-hydroxy-3-oxoheptanoate ((*R,S*)-**10j**): 0.92 g (81%) yield from aldehyde **9j** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure V; R_F 0.13 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ +45.1 (*c* 1.25, CH_2Cl_2); de = 95%, determined by NMR; ee = 94%, determined after *syn*-reduction and acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3090, 3063, 3027, 2957, 2899, 2862, 2719, 1747 (COOMe), 1716, 1654, 1632, 1588, 1561, 1495, 1474, 1460, 1439, 1405, 1390, 1366, 1325, 1256, 1203, 1161, 1102, 1078, 1050, 1011, 951, 929, 865, 822, 764, 701, 656. ^{1}H NMR: 1.06 s, 9 H (H-15); 2.60 dd, 1 H, *J*(7,7′) = 13.5, *J*(7,6) = 10.2 (H-7); 2.84–2.96 m, 2 H (H-4, H-4′); 3.05 ddd, 1 H, *J*(6,7) = 10.2, *J*(6,7′) = 4.4, *J*(6,5) = 3.8 (H-6); 3.15 dd, 1 H, *J*(7,7′) = 13.5, *J*(7′,6) = 4.4 (H-7′); 3.55 s br, 2 H (H-2, H-2′); 3.75 s, 3 H (OCH3); 4.29 m, 1 H (H-5); 7.18 dd, 1 H, *J*(12,13) = 8.2, *J*(12,10) = 1.9 (H-12); 7.24 d br, 1 H, *J*(13,12) = 8.2 (H-13); 7.35 d, 1 H, *J*(12,10) = 1.9 (H-10). ^{13}C NMR: 31.18 (C-15), 35.30 (C-7), 43.79 (C-14), 46.53 (C-4), 48.11 (C-6). 49.66 (C-2), 52.41 (OCH_3), 70.72 (C-5), 126.62 (C-12), 128.98 (C-13), 133.02 (C-11), 134.04 (C-10), 134.75 (C-9), 135.30 (C-8), 167.41 (C-1), 201.95 (C-3). MS (70 eV, *m/z* (rel.%)): 407 (0.1) [M^+], 388 (0.3) [$M^+ - H_2O$], 371 (18.2) [M^+ – Cl], 315 (3.9), 297 (12.9), 286 (0.8), 279 (2.9), 261 (4.9) [$C_{12}H_{15}Cl_2S^+$], 227 (4.3), 205 (18.2), 191 (3.2), 173 (36.9), 159 (15), 145 (21.9) [$C_6H_9O_4^+$], 134 (3), 113 (12), 101 (13.5), 85 (3.7), 75 (8.3), 57 (100) [$C_4H_9^+$], 43 (22.9) [$C_3H_7^+$], 41 (25) [$C_3H_5^+$]. For $C_{18}H_{24}Cl_2O_4S$ (407.4) calculated: 53.10% C, 5.94% H; found: 53.08% C, 6.17% H.

(+)-6-[(2R,3S)-3-(tert-Butylsulfanyl)-2-hydroxy-4-phenylbutyl]-2,2-dimethyl-4H-1,3-dioxin-4-one ((*R,S*)-**13i**): 1.05 g (86%) yield from aldehyde **9i** after column chromatography (silica gel, light petroleum/diethyl ether, 2:1) following procedure VI; R_F 0.27 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ +52.8 (*c* 0.78, CH_2Cl_2); de = 92%, determined by NMR; ee = 93%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (KBr): 3500–3200 (OH), 3082, 3062, 3026, 3002, 2974, 2963, 2939, 2899, 2858, 1947, 1865, 1707 (COO), 1636, 1494, 1470, 1455, 1438, 1421, 1392, 1357, 1341, 1326, 1308, 1283, 1256, 1206, 1182, 1152, 1084, 1072, 1057, 1027, 1018, 1006, 967, 935, 908, 879, 862, 840, 810, 708, 701, 638, 627. ^{1}H NMR: 1.21 s, 9 H (H-13); 1.67 s, 3 H (H-15); 1.68 s, 3 H (H-15′); 2.27 dd, 1 H, *J*(4,4′) = 14.6, *J*(4,5) = 10.2 (H-4); 2.53 dd, 1 H, *J*(4,4′) = 14.6, *J*(4′,5) = 3.0 (H-4′); 2.58 m, 1 H (OH); 2.86 dd, 1 H, *J*(7,7′) = 14.0, *J*(7,6) = 8.0 (H-7); 2.92 dd, 1 H, *J*(7,7′) = 14.0, *J*(7′,6) = 7.6 (H-7′); 3.06 ddd, 1 H, *J*(6,7) = 8.0, *J*(6,7′) = 7.6, *J*(6,5) = 3.8 (H-6); 3.95 m, 1 H (H-5); 5.32 s, 1 H (H-2); 7.19–7.36 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: 24.21 (C-15), 25.73 (C-15′), 31.34 (C-13), 37.46 (C-7), 40.31 (C-4), 43.95 (C-12), 51.84 (C-6), 69.20 (C-5), 95.35 (C-2), 106.63 (C-14), 126.71 (C-10), 128.42 (C-9), 129.32 (C-11), 138.54 (C-8), 161.04 (C-1), 169.18 (C-3). MS (70 eV, *m/z* (rel.%)): 364 (7.9) [M^+], 346 (1) [$M^+ - H_2O$], 307 (2.2) [$M^+ - C_4H_9$], 306 (9.3), 288 (24.3), 273 (0.8), 250 (10.3), 232 (29.9), 217 (5.3), 215 (3.3), 199 (5.9), 197 (2.3), 188 (7.3), 171 (3.7) [$M^+ - C_{12}H_{17}S$], 159 (33.7), 157 (4.5), 147 (4.3), 137 (62.6), 113 (24.3), 104 (11.9), 91 (43.6) [$C_7H_7^+$], 84 (10.2), 69 (22.3), 59 (46.5), 57 (100) [$C_4H_9^+$], 43 (23.2), 41 (28.8). For $C_{20}H_{28}O_4S$ (364.5) calculated: 65.90% C, 7.74% H; found: 66.10% C, 7.85% H.

(–)-2,2-Dimethyl-6-[(2R,3S)-2-hydroxy-4-methylpentyl-3-(phenylsulfanyl)]-1,3-4H-dioxin-4-one ((*R*,*S*)-**13j**): 0.94 g (89%) yield from aldehyde **9j** after column chromatography (silica gel, light petroleum/diethyl ether, 2:1) following procedure VI; R_F 0.21 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ –22.5 (*c* 1.17, CH_2Cl_2); de = 52%, determined by NMR; ee = 80%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (in $CHCl_3$): 3600–3200 (OH), 3078, 3060, 3015, 2963, 2872, 1950, 1875, 1718 (COO), 1634, 1584, 1480, 1462, 1439, 1392, 1378, 1277, 1258, 1216, 1128, 1088, 1062, 1018, 965, 906, 875, 808, 692, 668. ^{1}H NMR: 1.06 d, 3 H, *J*(8,7) = 6.6 (H-8); 1.30 d, 3 H, *J*(8′,7) = 6.6 (H-8′); 1.66 s br, 6 H (H-14, H-14′); 2.21 m, 1 H (H-7); 2.29 dd, 1 H, *J*(4,4′) = 14.5, *J*(4,5) = 9.9 (H-4); 2.70 dd, 1 H, *J*(4,4′) = 14.5, *J*(4′,5) = 3.0 (H-4′); 2.87 s br, 1 H (OH); 3.02 dd, 1 H, *J*(6,7) = 6.3, *J*(6,5) = 5.5 (H-6); 4.68 m, 1 H (H-5); 5.13 s br, 1 H (H-2); 7.18–7.48 m, 5 H (H-10, H-11, H-12). ^{13}C NMR: 19.11 (C-8), 21.50 (C-8′), 24.46 (C-14), 25.47 (C-14′), 29.34 (C-7), 38.56 (C-4), 64.42 (C-6), 69.75 (C-5), 95.20 (C-2), 106.68 (C-13), 126.88 (C-11), 129.15 (C-10), 131.08 (C-12), 136.38 (C-9), 161.27 (C-1), 169.57 (C-3). MS (70 eV, *m/z* (rel.%)): 336 (18) [M^+], 278 (38.8) [$M^+ - C_3H_6O$], 260 (31.7), 218 (1.9), 194 (12.4), 191 (15.3), 169 (6.1), 167 (12.1), 166 (74.2), 165 (100) [$C_{10}H_{13}S^+$], 151 (94.6), 135 (4.5), 123 (50.3), 113 (59.4), 110 (25.6), 109 (19.5), 91 (4.8) [$C_7H_7^+$], 87 (13.6), 85 (10.7), 69 (43.3), 65 (10), 57 (14.5), 55 (47.6), 45 (14.1), 43 (32.7) [$C_3H_7^+$], 41 (20.5). For $C_{18}H_{24}O_4S$ (336.5) calculated: 64.26% C, 7.19% H; found: 64.15% C, 7.34% H.

Methyl (3S,5R,6S)-(–)-6-(dibenzylamino)-3,5-dihydroxy-7-methyloctanoate ((*S*,*R*,*S*)-**11a**): 0.56 g (67%) yield from oxoester **10a** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure VII; R_F 0.30 (light petroleum/diethyl ether, 1:1); m.p. 78 °C; $[\alpha]_D^{20}$ –9.1 (*c* 0.63, CH_2Cl_2); de > 96%, determined by NMR; ee > 96%, determined after acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3100 (OH), 3085, 3062, 3023, 2954, 2872, 2801, 1950, 1883, 1825, 1728 (COOMe), 1602, 1562, 1494, 1453, 1439, 1403, 1363, 1270, 1217, 1160, 1095, 1070, 1028, 992, 969, 701. ^{1}H NMR: 0.94 d, 3 H, *J*(8,7) = 6.6 (H-8); 1.24 d, 3 H, *J*(8′,7) = 6.6 (H-8′); 1.56 ddd, 1 H, *J*(4,4′) = 14.0, *J*(4,3) = 11.0, *J*(4,5) = 9.3 (H-4); 1.76 ddd, 1 H, *J*(4,4′) = 14.0, *J*(4′,3) = 2.2, *J*(4′,5) = 1.6 (H-4′); 2.17 m, 1 H (H-7); 2.43 dd, 1 H, *J*(2,2′) = 15.8, *J*(2,3) = 5.5 (H-2); 2.51 dd, 1 H, *J*(6,7) = 9.3, *J*(6,5) = 5.5 (H-6); 2.53 dd, 1 H, *J*(2,2′) = 15.8, *J*(2′,3) 7.4 (H-2′); 3.67 s, 3 H (OCH_3); 3.74 d, 2 H, *J*(9,9′) = 13.5 (H-9); 3.87 d br, 2 H, *J*(9,9′) = 13.5 (H-9′); 4.20 m, 1 H (H-5), 4.26 m, 1 H (H-3); 7.22–7.36 m, 10 H (H-11, H-12, H-13). ^{13}C NMR: 20.68 (C-8), 23.18 (C-8′), 28.01 (C-7), 38.35 (C-4), 41.70 (C-2), 51.66 (OCH_3), 56.15 (C-9), 66.82 (C-6), 69.67 (C-3), 70.95 (C-5), 127.38 (C-12), 128.56 (C-10), 129.16 (C-13), 139.54 (C-10), 172.43 (C-1). MS (70 eV, *m/z* (rel.%)): 399 (0.2) [M^+], 356 (1) [$M^+ - C_3H_7$], 252 (35) [$C_6H_{11}O_4^+$], 181 (6), 160 (3), 91 (100) [$C_7H_7^+$], 84 (4), 65 (6), 43 (2), 41 (3). For $C_{24}H_{33}NO_4$ (399.5) calculated: 72.15% C, 8.32% H, 3.50% N; found: 72.15% C, 8.46% H, 3.77% N.

Methyl (3S,5R,6S)-(–)-6-(dibenzylamino)-3,5-dihydroxy-7,7-dimethyloctanoate ((*S*,*R*,*S*)-**11b**): 0.48 g (51%) yield from oxoester **10b** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure VII; R_F 0.38 (light petroleum/diethyl ether, 1:1); m.p. 86 °C; $[\alpha]_D^{20}$ –20.2 (*c* 1.4, CH_2Cl_2); de > 96%, determined by NMR; ee > 96%, determined after acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3100 (OH), 3085, 3063, 3024, 2954, 2872, 2799, 1950, 1880, 1810, 1728 (COOMe), 1602, 1494, 1453, 1439, 1358, 1271, 1174, 1094, 1074, 1028, 992, 758, 700. ^{1}H NMR: 1.06 s, 9 H (H-8); 1.64 ddd, 1 H, *J*(4,4′) = 14.3, *J*(4,3) = 2.2, *J*(4,5) = 2.1 (H-4); 1.84 ddd, 1 H, *J*(4,4′) = 14.3, *J*(4′,3) = 10.4,

J(4′,5) = 10.2 (H-4′); 2.41–2.49 m, 3 H (H-6, H-2, H-2′); 3.28–3.34 m br, 2 H (H-9); 3.72 s, 3 H (OCH_3); 3.81–4.11 m br, 2 H (H-9′); 4.16 m, 1 H (H-5); 4.21 m, 1 H (H-3); 7.20–7.36 m, 10 H (H-11, H-12, H-13). ^{13}C NMR: 29.89 (C-8), 37.36 (C-7), 41.48 (C-4), 43.12 (C-2), 51.82 (OCH_3), 56.78 (br, C-9), 69.10 (C-6), 69.95 (C-3), 72.65 (C-5), 126.90 (C-12), 128.19 (C-11), 129.26 (br, C-13), 140.17 (br, C-10), 172.92 (C-1). MS (70 eV, *m/z* (rel.%)): 412 (0.1) [$M^+ - 1$], 382 (1) [$M^+ - OCH_3$], 356 (20) [$M^+ - C(CH_3)_3$], 266 (36) [$C_{19}H_{24}N^+$], 181 (9), 162 (2), 106 (3), 91 (100) [$C_7H_7^+$], 65 (6), 57 (4), 43 (4), 41 (4). For $C_{25}H_{35}NO_4$ (413.6) calculated: 72.61% C, 8.53% H, 3.39% N; found: 72.71% C, 8.15% H, 3.61% N. HRMS $C_{21}H_{26}NO_4$ ($M^+ - C_4H_9$) calculated: 356.1862; found: 356.1862.

Methyl (3S,5R,6S)-(+)-6-(dibenzylamino)-3,5-dihydroxy-7-phenylheptanoate ((*S*,*R*,*S*)-**11c**): 0.61 g (61%) yield from oxoester **10c** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure VII; R_F 0.15 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ +11.6 (*c* 0.9, CH_2Cl_2); de > 96%, determined by NMR; ee > 96%, determined after acetalisation with 2,2-dimethoxypropane by ^1H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3085, 3062, 3026, 2951, 2843, 2803, 1950, 1877, 1810, 1734 (COOMe), 1602, 1585, 1495, 1453, 1439, 1365, 1309, 1255, 1217, 1170, 1104, 1073, 1051, 1029, 992, 973, 700. ^1H NMR: 1.47 ddd, 1 H, *J*(4,4′) = 14.0, *J*(4,3) = 10.4, *J*(4,5) = 10.2 (H-4); 1.82 dt, 1 H, *J*(4,4′) = 14.0, *J*(4′,3) = *J*(4′,5) = 2.2 (H-4′); 2.41 dd, 1 H, *J*(2,2′) = 16.2, *J*(2,3) = 5.2 (H-2); 2.47 dd, 1 H, *J*(2,2′) = 16.2, *J*(2′,3) = 7.4 (H-2′); 2.86 dd, 1 H, *J*(7,7′) = 13.5, *J*(7,6) = 6.3 (H-7); 2.98 ddd, 1 H, *J*(6,7′) = 6.9, *J*(6,7) = 6.3, *J*(6,5) = 4.9 (H-6); 3.09 dd, 1 H, *J*(7,7′) = 13.5, *J*(7′,6) = 6.9 (H-7′); 3.61 d br, 2 H, *J*(12,12′) = 13.7 (H-12); 3.69 s, 3 H (OCH_3); 3.77 d br, 2 H, *J*(12,12′) = 13.7 (H-12′); 3.95 ddd, 1 H, *J*(5,4) = 10.2, *J*(5,6) = 4.9, *J*(5,4′) = 2.2 (H-5); 4.16 dddd, 1 H, *J*(3,4) = 10.4, *J*(3,2′) = 7.4, *J*(3,2) = 5.2, *J*(3,4′) = 2.2 (H-3); 7.16–7.35 m, 15 H (H-9, H-10, H-11, H-14, H-15, H-16). ^{13}C NMR: 31.89 (C-7), 39.64 (C-4), 41.56 (C-2), 51.77 (OCH_3), 55.06 (C-12), 63.54 (C-6), 69.34 (C-3), 72.05 (C-5), 126.05 (C-11), 127.05 (C-16), 128.32 (C-10), 128.40 (C-15), 128.80 (C-12), 129.38 (C-17), 139.61 (C-9), 140.40 (C-14), 172.68 (C-1). MS (70 eV, *m/z* (rel.%)): 446 (0.2) [$M^+ - 1$], 416 (3) [$M^+ - OCH_3$], 356 (22) [$M^+ - C_7H_7$], 300 (100) [$C_{22}H_{22}N^+$], 265 (2), 208 (2), 181 (8), 132 (2), 91 (90) [$C_7H_7^+$], 65 (4), 45 (3). For $C_{28}H_{33}NO_4$ (447.6) calculated: 75.14% C, 7.43% H, 3.13% N; found: 75.52% C, 7.17% H, 3.61% N. HRMS $C_{27}H_{30}NO_3$ ($M^+ - OCH_3$) calculated: 416.2226; found: 416.2225.

Methyl (3S,5R,6S)-(+)-6-(tert-butyldimethylsilyl)-3,5-dihydroxy-7-phenylheptanoate ((*S*,*R*,*S*)-**11e**): 0.46 g (55%) yield from oxoester **10e** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure VII; R_F 0.19 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ +32.7 (*c* 0.6, CH_2Cl_2); de >96%, determined by NMR; ee = 93%, determined after acetalisation with 2,2-dimethoxypropane by ^1H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3083, 3061, 3025, 3001, 2954, 2929, 2883, 2856, 1950, 1870, 1737 (COOMe), 1602, 1495, 1454, 1438, 1363, 1252, 1221, 1162, 1091, 1030, 837, 825, 810, 767, 701. ^1H NMR: 0.06 s, 3 H (H-12); 0.15 s, 3 H (H-12′); 0.96 s, 9 H (H-14); 1.32 dt, 1 H, *J*(4,4′) = 14.3, *J*(4,5) = *J*(4,3) = 2.5 (H-4); 1.48 ddd, 1 H, *J*(6,7) = 10.2, *J*(6,7′) = 3.6, *J*(6,5) = 2.8 (H-6); 1.53 dt, 1 H, *J*(4,4′) = 14.3, *J*(4′,3) = *J*(4′,5) = 10.2 (H-4′); 2.25 dd, 1 H, *J*(2,2′) = 16.5, *J*(2,3) = 4.4 (H-2); 2.33 dd, 1 H, *J*(2.2′) = 16.5, *J*(2′,3) = 7.7 (H-2′); 2.73 dd, 1 H, *J*(7,7′) = 15.4, *J*(7,6) = 10.2 (H-7); 2.86 dd, 1 H, *J*(7,7′) = 15.4, *J*(7′,6) = 3.6 (H-7′); 3.00–3.50 s br, 2 H (OH); 3.66 s, 3 H (OCH_3); 4.03 dddd, 1 H, *J*(3,4′) = 10.2, *J*(3,2′) = 7.7, *J*(3,2) = 4.4, *J*(3,4) = 2.5 (H-3); 4.09 ddd, 1 H, *J*(6,4′) = 10.2, *J*(6,5) = 2.8, *J*(6,4) = 2.5 (H-6); 7.11–7.28 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: –5.74 (C-12), –5.30 (C-12′), 17.61 (C-13), 27.32 (C-14), 31.70 (C-6), 32.00 (C-7), 41.39 (C-4), 41.66 (C-2), 51.74 (OCH_3), 69.37

(C-3), 73.33 (C-5), 125.64 (C-11), 128.31 (C-10), 128.43 (C-12), 143.73 (C-9), 172.95 (C-1). MS (70 eV, *m/z* (rel.%)): 333 (1) [$M^+ - H_2O - CH_3$], 317 (1) [$M^+ - H_2O - CH_3O$], 291 (43) [$M^+ - H_2O - C_4H_9$], 277 (3) [$M^+ - CH_3OH - C_4H_9$], 259 (6) [$277^+ - H_2O$], 185 (21) [$291^+ - C_8H_{10}$], 167 (8), 157 (18), 143 (100), 129 (17), 117 (21) [$C_5H_9O_3^+$], 115 (10) [$TBDMS^+$], 107 (5), 91 (50) [$C_7H_7^+$], 89 (9), 75 (68) [$C_2H_7OSi^+$], 73 (31), 71 (8), 59 (9), 57 (5) [$C_4H_9^+$]. For $C_{20}H_{34}O_4Si$ (366.6) calculated: 65.53% C, 9.35% H; found: 65.83% C, 9.64% H.

Methyl (3S,5R,6S)-(+)-6-(tert-butyldimethylsilyl)-3,5-dihydroxy-7-(2,4-dichlorophenyl)heptanoate ((*S,R,S*)-**11f**): 0.41 g (52%) yield from oxoester **10f** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure VII; R_F 0.12 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ +30.7 (*c* 0.6, CH_2Cl_2); de > 96%, determined by NMR; ee = 95%, determined after acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3060, 3016, 2955, 2929, 2883, 2857, 2000, 1900, 1728 (COOMe), 1586, 1559, 1472, 1439, 1386, 1363, 1340, 1312, 1255, 1215, 1202, 1169, 1137, 1101, 1050, 1008, 935, 865, 825, 810, 759, 715, 702. ^{1}H NMR: 0.06 s, 3 H (H-14); 0.13 s, 3 H (H-14′); 0.96 s, 9 H (H-16); 1.32 ddd, 1 H, *J*(4,4′) = 14.3, *J*(4,3) = 2.7, *J*(4,5) = 2.2 (H-4); 1.42 ddd, 1 H, *J*(4,4′) = 14.3, *J*(4′,3) = 10.1, *J*(4′,5) = 9.6 (H-4′); 1.59 ddd, 1 H, *J*(6,7) = 11.3, *J*(6,7′) = 3.6, *J*(6,5) = 2.5 (H-6); 2.34 d, 2 H, *J*(2,3) = *J*(2′,3) = 6.0 (H-2, H-2′); 2.79 dd, 1 H, *J*(7,7′) = 15.1, *J*(7,6) = 3.6 (H-7); 2.96 dd, 1 H, *J*(7,7′) = 15.1, *J*(7′,6) = 11.3 (H-7′); 3.20 - 3.50 s br, 2 H (OH, OH′); 3.68 s, 3 H (CO_2CH_3); 4.03 ddd, 1 H, *J*(5,4′) = 9.6, *J*(5,6) = 2.5, *J*(5,4) = 2.2 (H-5); 4.07 ddt, 1 H, *J*(3,4′) = 10.1, *J*(3,4) = 2.7, *J*(3,2) = *J*(3,2′) = 6.0 (H-3); 7.16 dd, 1 H, *J*(12,13) = 8.2, *J*(12,10) = 2.2 (H-12); 7.26 d, 1 H, *J*(12,13) = 8.2 (H-13); 7.33 d, 1 H, *J*(10,12) = 2.2 (H-10). ^{13}C NMR: –5.71 (C-14), –5.29 (C-14′), 17.60 (C-15), 27.29 (C-18), 29.46 (C-7), 30.35 (C-6), 41.32 (C-4), 41.55 (C-2), 51.81 (OCH_3), 69.68 (C-3), 73.10 (C-5), 126.90 (C-12), 129.21 (C-13), 131.87 (C-10), 131.98 (C-11), 134.52 (C-9), 139.60 (C-8), 172.97 (C-1). MS (70 eV, *m/z* (rel.%)): 401 (0.9) [$M^+ - CH_3 - H_2O$], 385 (2) [$M^+ - H_2O - CH_3O$], 359 (56) [$M^+ - H_2O - C_4H_9$], 327 (7), 285 (3), 253 (12), 225 (17), 211 (61), 197 (8), 185 (8), 176 (9), 161 (35), 159 (58), 149 (6), 141 (5), 129 (5), 119 (11), 115 (10) [$TBDMS^+$], 107 (10), 105 (13),1 01 (4), 91 (10), 89 (24), 75 (100) [$C_2H_7OSi^+$], 73 (52) [TMS^+], 71 (17), 59 (14), 57 (15) [$C_4H_9^+$], 55 (13), 45 (16), 43 (60), 41 (14). For $C_{20}H_{32}Cl_2O_4Si$ (435.5) calculated: 55.16% C, 7.41% H; found: 54.90% C, 7.51% H.

Methyl (3S,5R,6S)-(+)-6-(tert-butylsulfanyl)-3,5-dihydroxy-7-phenylheptanoate ((*S,R,S*)-**11i**): 0.51 g (78%) yield from oxoester **10i** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure VII; R_F 0.14 (light petroleum/diethyl ether, 2:1); m.p. 75–76 °C; 35.0 (*c* 0.6, CH_2Cl_2); de = 80%, determined by NMR; ee = 93%, determined after acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3100 (OH), 3080, 3061, 3031, 2968, 2955, 2862, 1737 (COOMe), 2686, 1677, 1655, 1648, 1637, 1618, 1603, 1561, 1523, 1509, 1498, 1445, 1377, 1366, 1335, 1294, 1245, 1202, 1164, 1108, 1072, 1049, 1031, 1005, 935, 858, 750, 705. ^{1}H NMR: 1.19 s, 9 H (H-13); 1.65 ddd, 1 H, *J*(4,4′) = 14.1, *J*(4,5) = 10.4, *J*(4,3) = 9.1 (H-4); 1.83 ddd, 1 H, *J*(4,4′) = 14.1, *J*(4′,3) = 3.3, *J*(4′,5) = 2.4 (H-4′); 2.47 dd, 1 H, *J*(2,2′) = 16.2, *J*(2,3) = 5.2 (H-2); 2.54 dd, 1 H, *J*(2,2′) = 16.2, *J*(2′,3) = 7.4 (H-2′); 2.82–3.01 m, 3 H (H-6, H-7, H-7′); 3.14 s br, 1 H (OH); 3.71 s, 3 H (OCH_3); 3.88 s br, 2 H (OH′, H-5); 4.24 dddd, 1 H, *J*(3,4) = 9.1, *J*(3,2′) = 7.4, *J*(3,2) = 5.2, *J*(3,4′) = 3.3 (H-3); 7.19–7.32 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: 31.38 (C-13), 38.30 (C-7), 39.56 (C-4), 41.45 (C-2), 43.64 (C-12), 51.75 (OCH_3), 51.88 (C-6), 68.41 (C-3), 72.72 (C-5), 126.44 (C-10), 130.07 (C-9), 135.68 (C-11), 143.73 (C-8), 172.56 (C-1). MS (70 eV, *m/z* (rel.%)): 340 (1) [M^+], 323 (2) [$M^+ - H_2O$], 322 (1) [$M^+ - H_2O$], 291 (2) [$M^+ - CH_3O - H_2O$], 235 (3) [$291^+ -$

C_4H_8], 219 (5) [$M^+ - CH_3OH - SC_4H_9$], 201 (54) [$219^+ - H_2O$], 194 (31) [$250^+ - C_4H_8$], 193 (8) [$M^+ - C_6H_{11}O_4$], 175 (16), 159 (25) [$201^+ - H_2C{=}C{=}O$], 147 (14) [$C_6H_{11}O_4^+$], 138 (27) [$194^+ - C_4H_8$], 137 (44) [$194^+ - C_4H_9$], 129 (47) [$147^+ - H_2O$], 115 (9) [$147^+ - CH_3OH$], 103 (16) [$194^+ - C_7H_7$], 97 (22) [$C_5H_5O_2^+$], 91 (50) [$C_7H_7^+$], 73 (23), 57 (100) [$C_4H_9^+$], 43 (10) [$C_3H_7^+$], 41 (17) [$C_3H_5^+$]. For $C_{18}H_{28}O_4S$ (340.5) calculated: 63.50% C, 8.29% H; found: 63.53% C, 8.27% H.

Methyl (3S,5R,6S)-(+)-6-(tert-butylsulfanyl)-7-(2,4-dichlorophenyl)-3,5-dihydroxyheptanoate ((*S,R,S*)-**11j**): 0.73 g (86%) yield from oxoester **10j** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure VII; R_F 0.18 (light petroleum/diethyl ether, 2:1); $[\alpha]_D^{20}$ +9.4 (*c* = 0.6, CH_2Cl_2); de = 80%, determined by NMR; ee = 94%, determined after acetalisation with 2,2-dimethoxypropane by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3700–3200 (OH), 3080, 3060, 3006, 2963, 2935, 2872, 1950, 1870, 1718 (COOMe), 1634, 1584, 1480, 1439, 1392, 1378, 1277, 1258, 1215, 1205, 1128, 1058, 1063, 1018, 965, 906, 875, 839, 808, 692. ^{1}H NMR: 1.07 s, 9 H (H-15); 1.78 ddd, 1 H, *J*(4,4′) = 14.3, *J*(4,5) = 9.6, *J*(4,3) = 9.1 (H-4); 1.85 ddd, 1 H, *J*(4,4′) = 14.3, *J*(4′,3) = 3.3, *J*(4′,5) = 3.0 (H-4′); 2.51 dd, 1 H, *J*(2,2′) = 15.9, *J*(2,3) = 4.9 (H-2); 2.59 dd, 1 H, *J*(2,2′) = 15.9, *J*(2′,3) = 7.4 (H-2′); 2,66 dd, 1 H, *J*(7,7′) = 13.5, *J*(7,6) = 10.4 (H-7); 3.01 ddd, 1 H, *J*(6,7) = 10.4, *J*(6,7′) = 4.7, *J*(6,5) = 3.3 (H-6); 3.15 dd, 1 H, *J*(7,7′) = 13.5, *J*(7′,6) = 4.7 (H-7′); 3.32 s br, 1 H (OH); 3.90 s br, 1 H (OH′); 4.02 ddd, 1 H, *J*(5,4) = 9.6, *J*(5,6) = 3.3, *J*(5,4′) = 3.0 (H-5); 4.30 dddd, 1 H, *J*(3,4) = 9.1, *J*(3,2′) = 7.4, *J*(3,2) = 4.9, *J*(3,4′) = 3.3 (H-3); 7.17 dd, 1 H, *J*(12,13) = 8.2, *J*(12,10) = 1.9 (H-12); 7.23 d br, 1 H, *J*(13,12) = 8.2 (H-13); 7.35 d, 1 H, *J*(10,12) = 1.9 (H-10). ^{13}C NMR: 31.19 (C-15), 35.35 (C-7), 38.81 (C-4), 41.53 (C-2), 43.55 (C-14), 48.94 (C-6), 51.76 (OCH_3), 68.43 (C-3), 74.59 (C-5), 126.52 (C-12), 128.97 (C-13), 132.92 (C-11), 134.03 (C-10), 134.73 (C-9), 135.53 (C-8), 172.60 (C-1). MS (70 eV, *m/z* (rel.%)): 408 (0.2) [M^+], 373 (11) [M^+ – Cl], 341 (1) [$373^+ - CH_3OH$], 317 (1) [$373^+ - C_4H_8$], 299 (5) [$317^+ - H_2O$], 285 (4) [$341^+ - C_4H_8$], 261 (3) [$M^+ - C_6H_{11}O_4$], 227 (17) [$261^+ - H_2S$], 205 (10) [$261^+ - C_4H_8$], 171 (10), 159 (14) [$C_7H_5Cl_2^+$], 147 (13) [$C_6H_{11}O_4^+$], 143 (6), 129 (46) [$147^+ - H_2O$], 115 (5) [$147^+ - CH_3OH$], 103 (8), 97 (25) [$C_5H_5O_2^+$], 71 (8), 57 (100) [$C_4H_9^+$], 43 (16) [$C_3H_7^+$], 41 (28). HRMS $C_{18}H_{26}ClO_4S$ (M^+ – Cl) calculated: 373.1240; found: 373.1239.

(6R)-(–)-6-[(1S)-(Dibenzylamino)-3-methylbutyl]-4-hydroxy-5,6-dihydropyran-2-one ((*S,R*)-**14d**): 0.54 g (76%) yield from δ-hydroxy-β-ketoester **10d** after column chromatography (silica gel, light petroleum/diethyl ether, 1:2) following procedure VIII; R_F 0.23 (light petroleum/diethyl ether, 1:2); $[\alpha]_D^{20}$ –21.7 (*c* 0.45, CH_2Cl_2); m.p. 80 °C (dec.); de = 95%, determined by NMR; ee > 96%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (KBr): 3700–2400, 3084, 3061, 3026, 2951, 2867, 2843, 2817, 2744, 2693, 2637, 2582, 1958, 1871, 1814, 1750 (CO), 1719 (COO), 1646, 1613, 1584, 1494, 1481, 1467, 1455, 1413, 1400, 1382, 1367, 1354, 1295, 1248, 1230, 1195, 1170, 1120, 1045, 1038, 982, 957, 925, 882, 828, 755, 735, 702. ^{1}H NMR: 0.75 d, 3 H, *J*(9,8) = 6.6 (H-9); 0.94 d, 3 H, *J*(9′,8) = 6.6 (H-9′); 1.34 ddd, 1 H, *J*(7,7′) = 13.5, *J*(7,8) = 8.5, *J*(7,6) = 5.2 (H-7); 1.84 m, 1 H (H-7′); 1.97 m, 1 H (H-8); 2.34 dd, 1 H, *J*(4,4′) = 18.7, *J*(4,5) = 11.5 (H-4); 2.73 m, 1 H (H-6); 3.53 d br, 1 H, *J*(4,4′) = 18.7 (H-4′); 3.60 d br, 2 H, *J*(10,10′) = 14.0 (H-10); 3.78 d br, 2 H, *J*(10,10′) = 14.0 (H-10′); 4.62 s br, 1 H (H-2); 4.75 ddd, 1 H, *J*(5,4) = 11.5, *J*(5,6) = 5.0, *J*(5,4) = 2.7 (H-5); 7.21–7.35 m, 10 H (H-12, H-13, H-14). ^{13}C NMR: 23.00 (C-9), 23.90 (C-9′), 25.76 (C-8), 36.32 (C-7), 42.83 (C-4), 47.72 (C-2), 55.11 (C-10), 58.13 (C-6), 76.46 (C-5), 127.92 (C-13), 129.06 (C-12), 129.51 (C-14), 139.73 (C-11), 167.76 (C-1), 200.90 (C-3). MS (70 eV, *m/z* (rel.%)): 379 (0.1) [M^+], 278 [M^+ – 101], 266 (20) [$M^+ - C_5H_5O_3^+$], 181 (2), 118

(1), 91 (100) [$C_7H_7^+$], 77 (1), 65 (8), 44 (7). For $C_{24}H_{29}NO_3$ (379.5) calculated: 75.96% C, 6.90% H, 3.69% N; found: 75.63% C, 6.78% H, 3.89% N.

(6R)-(–)-6-[(1S)-(Dibenzylamino)-3-methylbutyl]-4-methoxy-5,6-dihydropyran-2-one ((*S*,*R*)-**15d**): 0.64 g (86%) yield from 4-oxo-5,6-dihydropyrane **14d** after column chromatography (silica gel, light petroleum/diethyl ether, 1:2) following procedure VIII; R_F 0.39 (light petroleum/diethyl ether, 1:2); $[\alpha]_D^{20}$ –8.2 (*c* 0.56, CH_2Cl_2); m.p. 92 °C; de = 95%, determined by NMR; ee > 96%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (KBr): 3105, 3084, 3062, 3028, 2928, 2924, 2866, 2813, 1713, 1635, 1545, 1494, 1468, 1455, 1384, 1343, 1319, 1292, 1252, 1227, 1200, 1181, 1120, 1081, 1068, 1039, 999, 973, 955, 835, 753, 733, 702, 676, 663. ^{1}H NMR: 0.72 d, 3 H, *J*(9,9′) = 6.4 (H-9); 0.92 d, 3 H, *J*(9′,8) = 6.7 (H-9′); 1.34 ddd, 1 H, *J*(7,7′) = 14.3, *J*(7,8) = 7.9, *J*(7,6) = 5.2 (H-7); 1.77 ddd, 1 H, *J*(7,7′) = 14.3, *J*(7′,6) = 7.6, *J*(7′,8) = 5.8 (H-7′); 1.96 m, 1 H (H-8); 2.35 dd, 1 H, *J*(4,4′) = 17.1, *J*(4,5) = 4.3 (H-4); 2.46 ddd, 1 H, *J*(4,4′) = 17.1, *J*(4′,5) = 11.5, *J*(4′,2) = 1.5 (H-4′), 2.75 dt, 1 H, *J*(6,7′) = 7.6, *J*(6,5) = *J*(6,7) = 5.2 (H-6); 3.57 d br, 2 H, *J*(10,10′) = 13.7 (H-10); 3.69 s, 3 H (OCH_3); 3.77 d br, 2 H, *J*(10,10′) = 14.0 (H-10′); 4.64 ddd, 1 H, *J*(5,4′) = 11.5, *J*(5,6) = 5.2, *J*(5,4) = 4.3 (H-5); 5.09 d, 1 H, *J*(2,4′) = 1.5 (H-2); 7.21–7.32 m, 10 H (H-12, H-13, H-14). ^{13}C NMR: 22.39 (C-9), 23.41 (C-9′), 25.06 (C-8), 31.40 (C-4), 35.86 (C-7), 54.32 (C-10), 55.90 (OCH_3), 57.16 (C-6), 75.74 (C-5), 90.15 (C-2), 127.21 (C-13), 128.28 (C-12), 128.94 (C-14), 139.66 (C-11), 167.21 (C-3), 172.98 (C-1). MS (70 eV, *m/z* (rel.%)): 266 (44) [$C_{19}H_{24}N^+$], 181 (6), 174 (3), 92 (7), 91 (100) [$C_7H_7^+$], 65 (7), 42 (9). For $C_{25}H_{31}NO_3$ (393.5) calculated: 76.30% C, 7.94% H, 3.56% N; found: 76.51% C, 8.32% H, 3.57% N.

(6R)-(+)-6-[(1S)-(tert-Butylsulfanyl)-2-phenylethyl]-4-methoxy-5,6-dihydropyran-2-one ((*S*,*R*)-**16i**): 1,3-dioxine **13i** (0.29 g, 0.8 mmol) was dissolved in methanol (5 ml) and potassium carbonate (0.22 g, 1.6 mmol) was added at room temperature while stirring. After stirring for 12 h the reaction mixture was subsequently neutralised with 1 M aqueous hydrochloric acid. Standard aqueous work-up with diethyl ether (30 ml/mmol) and water (3 ml/mmol) resulted in the ketoester **10i** which was subsequently submitted to procedure VIII to yield 0.22 g (85%) of a colourless solid after column chromatography (silica gel, light petroleum/diethyl ether, 1:1); R_F 0.22 (light petroleum/diethyl ether, 1:1); $[\alpha]_D^{20}$ +51.4 (*c* 0.65, CH_2Cl_2); m.p. 114–116 °C; de = 93%, determined by NMR; ee = 93%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR ($CHCl_3$): 3086, 3060, 3014, 2960, 2941,2926, 2900, 2860, 1713, 1625, 1603, 1495, 1457, 1444, 1418, 1388, 1366, 1357, 1292, 1238, 1219, 1162, 1055, 994, 959, 890, 825, 703, 667. ^{1}H NMR: 1.15 s, 9 H (H-13); 2.49 dd, 1 H, *J*(4,4′) = 17.0, *J*(4,5) = 3.9 (H-4); 2.70 ddd, 1 H, *J*(4,4′) = 17.0, *J*(4′,5) = 12.1, *J*(4′,2) = 1.7 (H-4′); 2.94 m, 2 H (H-7, H-7′); 3.06 dt, 1 H, *J*(6,7) = *J*(6,7′) = 7.2, *J*(6,5) = 6.4 (H-6); 3.65 s, 3 H (OCH_3); 4.23 ddd, 1 H, *J*(5,4′) = 12.1, *J*(5,6) = 6.4, *J*(5,4) = 3.9 (H-5); 5.05 d, 1 H, *J*(2,4′) = 1.7 (H-2); 7.10–7.23 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: 30.68 (C-7), 32.02 (C-13), 40.05 (C-4), 44.75 (C-6), 47.94 (C-6), 56.64 (OCH_3), 78.05 (C-5), 90.74 (C-2), 127.28 (C-10), 128.84 (C-9), 130.58 (C-11), 138.60 (C-8), 167.50 (C-1), 173.67 (C-3). MS (70 eV, *m/z* (rel.%)): 320 (5) [M^+], 263 (8) [$M^+ - C_4H_9$], 231 (4) [$M^+ - SC_4H_9$], 194 (11) [$M^+ - C_{12}H_{18}S^+$], 193 (15) [$M^+ - C_6H_7O_3^+$], 173 (12), 137 (28), 127 (100) [$C_6H_7O_3^+$], 115 (10), 91 (35) [$C_7H_7^+$], 57 (62), 43 (23), 41 (35). For $C_{25}H_{31}NO_3$ (393.5) calculated: 76.30% C, 7.94% H, 3.56% N; found: 76.51% C, 8.32% H, 3.57% N.

Methyl (4S,6R)-(–)-6-[(1S)-(dibenzylamino)-2-methylpropyl]-2,2-dimethyl-1,3-dioxane-4-acetate ((*S*,*S*,*R*)-**17a**): 0.32 g (55%) yield from dihydroxyester **11a** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure IX; R_F 0.70 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ –40.6 (*c* 0.9, CH_2Cl_2); de > 96%, determined by NMR; ee =

95%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3064, 3062, 3024, 2994, 2975, 2947, 2898, 2837, 2814, 1953, 1870, 1742 (COOMe), 1601, 1494, 1453, 1442, 1383, 1355, 1287, 1238, 1204, 1168, 1131, 1110, 1093, 1071, 1051, 1017, 981, 966, 950, 919, 906, 887, 866, 850, 810, 755, 740, 700. ^{1}H NMR: 1.00 d, 3 H, *J*(8,7) = 6.9 (H-8); 1.10 d, 3 H, *J*(8′,7) = 6.9 (H-8′); 1.20 ddd, 1 H, *J*(4,4′) = 12.9, *J*(4,5) = 11.8, *J*(4,3) = 11.5 (H-4); 1.32 s, 3 H (H-10); 1.49 s, 3 H (H-10′); 1.76 dt, 1 H, *J*(4,4′) = 12.9, *J*(4′,5) = *J*(4′,3) = 2.5 (H-4′); 2.20 m, 1 H (H-7); 2.29 dd, 1 H, *J*(6,7) = 6.3, *J*(6,5) = 4.4 (H-6); 2.39 dd, 1 H, *J*(2,2′) = 15.4, *J*(2,3) = 6.0 (H-2); 2.53 dd, 1 H, *J*(2,2′) = 15.4, *J*(2′,3) = 7.1 (H-2′); 3.61 d br, 2 H, *J*(11,11′) = 13.7 (H-11); 3.67 d br, 2 H, *J*(11,11′) = 13.7 (H-11′); 3.71 s, 3 H (OCH_3); 4.28 m, 1 H (H-5); 4.33 m, 1 H (H-3); 7.21–7.35 m, 10 H (H-13, H-14, H-15). ^{13}C NMR: 19.32 (C-10), 20.01 (C-8), 23.15 (C-8′), 25.59 (C-7), 30.03 (C-10′), 35.84 (C-4), 41.45 (C-2), 51.61 (OCH_3), 54.78 (C-11), 65.19 (C-6), 66.49 (C-3), 67.27 (C-5), 98.56 (C-9), 126.83 (C-14), 128.14 (C-13), 128.96 (C-15), 140.05 (C-12), 171.50 (C-1). MS (70 eV, *m/z* (rel.%)): 439 (0.5) [M^+], 424 (5) [$M^+ - CH_3$], 396 (6) [$M^+ - CH_3CO$], 338 (3), 308 (2), 252 (100) [$C_{18}H_{22}N^+$], 210 (5), 181 (7), 160 (3), 91 (61) [$C_7H_7^+$], 65 (5), 55 (6), 43 (12) [$C_3H_7^+$]. HRMS $C_{18}H_{24}O_3S$ (M^+) calculated: 320.14462; found: 320.14429.

Methyl (4S,6R)-(–)-6-[(1S)-(dibenzylamino)-2,2-dimethylpropyl]-2,2-dimethyl-1,3-dioxane-4-acetate ((*S,S,R*)-**17b**): 0.49 g (68%) yield from dihydroxyester **11b** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure IX; R_F 0.54 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ –43.4 (*c* 0.8, CH_2Cl_2); de > 96%, determined by NMR; ee > 95%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3085, 3062, 3025, 2990, 2952, 2871, 2798,1945, 1871, 1800, 1740 (COOMe), 1602, 1585, 1543, 1494, 1454, 1438, 1396, 1381, 1363, 1315, 1262, 1201, 1166, 1121, 1099, 1076, 1028, 1001, 947, 933, 796, 700. ^{1}H NMR: 0.99 s, 9 H (H-8); 1.36 s, 3 H (H-10); 1.49 s, 3 H (H-10′); 1.46–1.58 m, 1 H (H-4); 2.35 d, 1 H, *J*(6,5) = 2.7 (H-6); 2.37 dd, 1 H, *J*(2,2′) = 15.3, *J*(2,3) = 7.1 (H-2); 2.53 dd, 1 H, *J*(2,2′) = 15.3, *J*(2′,3) = 7.1 (H-2′); 3.49–3.65 m br, 2 H (H-11); 3.71 s, 3 H (OCH_3); 3.80–4.20 m br, 2 H (H-11′); 4.20–4.35 m, 2 H (H-5, H-3); 7.20–7.45 m br, 10 H (H-13, H-14, H-15). Note: H-4′ was not observed. ^{13}C NMR: 19.12 (C-10), 29.65 (C-8), 30.08 (C-10′), 37.14 (C-7), 37.41 (C-4), 41.28 (C-2), 51.63 (OCH_3), 56.00–58.00 (br C-11), 66.82 (C-6), 67.80 (C-3), 68.86 (C-5), 98.84 (C-9), 126.82 (C-14), 128.06 (C-13), 129.31 (br C-15), 140.00–141.00 (br C-12), 171.44 (C-1). MS (70 eV, *m/z* (rel.%)): 453 (0.2) [M^+], 438 (3) [$M^+ - CH_3$], 396 (39) [$M^+ - C(CH_3)_3$], 378 (4) [396 – H_2O], 364 (3) [$396^+ - CH_3OH$], 338 (14), 266 (40) [$C_{19}H_{24}N^+$], 246 (5), 210 (19), 181 (7), 91 (100) [$C_7H_7^+$], 59 (5), 57 (4) [$C_4H_9^+$], 43 (5), 41 (5). HRMS $C_{24}H_{30}NO_4$ ($M^+ - C_4H_9$) calculated: 396.2175; found: 396.2175.

Methyl (4S,6R)-(–)-6-[(1S)-(dibenzylamino)-2-phenylethyl]-2,2-dimethyl-1,3-dioxane-4-acetate ((*S,S,R*)-**17c**): 0.56 g (81%) yield from dihydroxyester **11c** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure IX; R_F 0.38 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ –25.9 (*c* 0.7, CH_2Cl_2); de > 96%, determined by NMR; ee > 96%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3085, 3062, 3026, 2993, 2949, 2801, 1949, 1872, 1808, 1740 (COOMe), 1603, 1495, 1454, 1438, 1381, 1315, 1260, 1201, 1168, 1120, 1076, 1029, 983, 946, 699. ^{1}H NMR: 1.06 ddd, 1 H, *J*(4,4′) = 12.6, *J*(4,5) = 11.8, *J*(4,3) = 11.2 (H-4); 1.34 s, 3 H (H-13); 1.50 s, 3 H (H-13′); 1.56 ddd, 1 H, *J*(4,4′) = 12.6, *J*(4′,5) = 2.5, *J*(4′,3) = 2.2 (H-4′); 2.33 dd, 1 H, *J*(2,2′) = 15.4, *J*(2,3) = 5.8 (H-2); 2.49 dd, 1 H, *J*(2,2′) = 15.4, *J*(2′,3) = 7.1 (H-2′); 2.82 ddd, 1 H, *J*(6,7) = 8.2, *J*(6,7′) = 4.9, *J*(6,5) = 4.1 (H-6); 2.92 dd, 1 H, *J*(7,7′) = 14.3, *J*(7′,6) = 4.9 (H-7′); 2.97 dd, 1 H, *J*(7,7′) = 14.3, *J*(7,6) = 8.2 (H-7); 3.63 d br, 2 H, *J*(14,14′) = 14.0 (H-14);

3.68 s, 3 H (OCH_3); 3.70 d br, 2 H, *J*(14,14′) = 14.0 (H-14′); 4.21 ddd, 1 H, *J*(5,4) = 11.8, *J*(5,6) = 4.1, *J*(5,4′) = 2.5 (H-5); 4.30 dddd, 1 H, *J*(3,4) = 11.2, *J*(3,2′) = 7.1, *J*(3,2) = 5.8, *J*(3,4′) = 2.2 (H-3); 7.10–7.28 m, 15 H (H-9, H-10, H-11, H-16, H-17, H-18). ^{13}C NMR: 19.67 (C-13), 30.02 (C-13′), 32.09 (C-7), 34.84 (C-4), 41.35 (C-2), 51.64 (OCH_3), 54.63 (C-14), 63.25 (C-6), 66.26 (C-3), 69.04 (C-5), 98.70 (C-12), 125.58 (C-10), 126.72 (C-17), 128.00 (C-9), 128.08 (C-16), 128.65 (C-11), 129.72 (C-18), 140.00 (C-8), 141.59 (C-15), 171.46 (C-1). MS (70 eV, *m/z* (rel.%)): 453 (0.2) [M^+], 438 (3) [$M^+ - CH_3$], 396 (39) [$M^+ - C(CH_3)_3$], 378 (4) [396 – H_2O], 364 (3) [$396^+ - CH_3OH$], 338 (14), 266 (40) [$C_{19}H_{24}N^+$], 246 (5), 210 (19), 181 (7), 91 (100) [$C_7H_7^+$], 59 (5), 57 (4) [$C_4H_9^+$], 43 (5), 41 (5). HRMS $C_{24}H_{30}NO_4$ ($M^+ - C_4H_9$) calculated: 396.2175; found: 396.2175.

Methyl (4S,6R)-(+)-6-[(1S)-(tert-butyldimethylsilyl)-2-phenylethyl]-2,2-dimethyl-1,3-dioxane-4-acetate ((*S,S,R*)-**17e**): 0.61 g (90%) yield from dihydroxyester **11e** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure IX; R_F 0.48 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ +34.3 (*c* 0.8, CH_2Cl_2); de > 96%, determined by NMR; ee > 93%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3084, 3062, 3025, 2992, 2954, 2930, 2882, 2856, 1945, 1875, 1743 (COOMe), 1602, 1464, 1455, 1438, 1380, 1362, 1326, 1325, 1258, 1200, 1167, 1120, 1102, 1050, 1032, 1002, 953, 873, 824, 809, 767, 699. ^{1}H NMR: 0.04 s, 3 H (H-13); 0.08 s, 3 H (H-13′); 0.93 s, 9 H (H-16); 1.14–1.32 m, 2 H (H-4, H-4′); 1.35 s br, 6 H (H-13, H-13′); 1.46 ddd, 1 H, *J*(6,7) = 7.4, *J*(6,7′) = 5.8, *J*(6,5) = 3.0 (H-6); 2.23 dd, 1 H, *J*(2,2′) = 15.7, *J*(2,3) = 5.8 (H-2); 2.41 dd, 1 H, *J*(2,2′) = 15.7, *J*(2′,3) = 7.4 (H-2′); 2.80–2.82 m, 2 H (H-7, H-7′); 3.64 s, 3 H (OCH_3); 4.05 m, 1 H (H-5); 4.14 m, 1 H (H-3); 7.10–7.30 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: –5.65 (C-14), –5.33 (C-14′), 17.66 (C-15), 19.68 (C-13), 27.38 (C-16), 29.74 (C-6), 29.99 (C-13′), 31.60 (C-7), 35.18 (C-4), 41.24 (C-2), 51.55 (OCH_3), 66.21 (C-3), 69.85 (C-5), 98.60 (C-12), 125.52 (C-10), 128.24 (C-9), 128.37 (C-11), 143.76 (C-8), 171.52 (C-1). MS (70 eV, *m/z* (rel.%)): 406 (0.2) [M^+], 391 (1) [$M^+ - CH_3$], 349 (1) [$M^+ - C_4H_9$], 291 (100) [$349^+ - CH_3COCH_3$], 259 (12) [$291^+ - CH_3OH$], 217 (2), 191 (8), 185 (8), 167 (9), 157 (6), 143 (36), 129 (8), 128 (6), 117 (6), 115 (9) [TBDMS$^+$], 91 (28) [$C_7H_7^+$], 89 (28), 75 (29) [$C_2H_7OSi^+$], 73 (29) [TMS$^+$], 59 (10), 57 (8) [$C_4H_9^+$], 55 (7), 43 (7), 41 (9). HRMS $C_{22}H_{35}O_4Si$ ($M^+ - CH_3$) calculated: 391.2305; found: 391.2307.

Methyl (4S,6R)-(+)-6-[(1S)-(tert-butyldimethylsilyl)-2-(2,4-dichlorophenyl)ethyl]-2,2-dimethyl-1,3-dioxane-4-acetate ((*S,S,R*)-**17f**): 0.59 g (90%) yield from dihydroxyester **11f** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure IX; R_F 0.64 (light petroleum/diethyl ether, 4:1); $[\alpha]_D^{20}$ +36.5 (*c* 0.8, CH_2Cl_2); de = 95%, determined by NMR; ee = 95%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3095, 3060, 3020, 2954, 2929, 2883, 2857, 1900, 1729 (COOMe), 1586, 1559, 1472, 1439, 1387, 1363, 1338, 1310, 1255, 1201, 1169, 1137, 1101, 1050, 1008, 865, 825, 810, 715, 702, 689, 667. ^{1}H NMR: 0.05 s, 3 H (H-15); 0.08 s, 3 H (H-15′); 0.93 s, 9 H (H-18); 1.02 ddd, 1 H, *J*(4,4′) = 12.6, *J*(4,5) = 11.6, *J*(4,3) = 11.5 (H-4); 1.22 ddd, 1 H, *J*(4,4′) = 12.6, *J*(4′,3) = 2.7, *J*(4′,5) = 2.4 (H-4′); 1.34 s, 3 H (H-15); 1.36 s, 3 H (H-15′); 1.52 ddd, 1 H, *J*(6,7) = 11.0, *J*(6,7′) = 3.1, *J*(6,5) = 2.7 (H-6); 2.20 dd, 1 H, *J*(2,2′) = 15.6, *J*(2,3) = 5.8 (H-2); 2.37 dd, 1 H, *J*(2,2′) = 15.6, *J*(2′,3) = 7.0 (H-2′); 2.77 dd, 1 H, *J*(7,7′) = 15.6, *J*(7′,6) = 3.1 (H-7′); 2.98 dd, 1 H, *J*(7,7′) = 15.6, *J*(7,6) = 11.0 (H-7); 3.64 s, 3 H (OCH_3); 4.03 ddd, 1 H, *J*(5,4) = 11.6, *J*(5,6) = 2.7, *J*(5,4′) = 2.4 (H-5); 4.13 dddd, 1 H, *J*(3,4) = 11.5, *J*(3,2′) = 7.0, *J*(3,2) = 5.8, *J*(3,4′) = 2.7 (H-3); 7.16 dd, 1 H, *J*(12,13) = 8.2, *J*(12,10) = 2.1 (H-12); 7.25 d, 1 H, *J*(13,12) = 8.2 (H-13); 7.33 d, 1 H, *J*(10,12) = 2.1 (H-10). ^{13}C NMR: –5.65 (C-16), –5.49 (C-16′), 17.64 (C-17), 19.61 (C-15), 27.35 (C-18), 28.45 (C-6), 28.99 (C-7),

29.99 (C-15′), 35.43 (C-4), 41.16 (C-2), 51.57 (OCH_3), 66.17 (C-3), 69.48 (C-5), 98.70 (C-14), 126.69 (C-12), 129.19 (C-13), 131.61 (C-10), 131.83 (C-11), 134.58 (C-9), 139.72 (C-8), 171.44 (C-1). MS (70 eV, *m/z* (rel.%): 459 (0.8) [$M^+ - CH_3$], 401 (3) [$M^+ - C_3H_5O_2$], 359 (74) [$M^+ - C_4H_9 - CH_3COCH_3$], 327 (8) [$359^+ - CH_3OH$], 259 (5) [$C_{11}H_{13}Cl_2OSi^+$], 225 (4), 211 (14), 203 (8), 185 (8), 159 (34), 133 (7), 119 (45), 115 (13) [$TBDMS^+$], 105 (6), 93 (17), 89 (100) [$C_4H_7O_2^+$], 75 (69) [$C_2H_7OSi^+$], 73 (87) [TMS^+], 69 (6), 57 (10) [$C_4H_9^+$], 43 (22), 41 (15.5). For $C_{23}H_{36}Cl_2O_4Si$ (475.5) calculated: 58.09% C, 7.63% H; found: 58.47% C, 7.71% H.

Methyl (4S,6R)-(+)-6-[(1S)-(tert-butylsulfanyl)-2-phenylethyl]-2,2-dimethyl-1,3-dioxane-4-acetate ((*S,S,R*)-**17i**): 0.52 g (83%) yield from dihydroxyester **11i** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure IX; R_F 0.50 (light petroleum/diethyl ether, 4:1); m.p.: 110 °C (pentane); $[\alpha]_D^{20}$ +15.5 (*c* 0.52, CH_2Cl_2). de > 96%, determined by NMR; ee = 93%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3084, 3066, 3027, 2980, 2962, 2932, 2874, 1937, 1861, 1736 (COOMe), 1605, 1495, 1473, 1460, 1445, 1409, 1391, 1380, 1364, 1322, 1252, 1230, 1198, 1166, 1148, 1126, 1065, 1039, 1030, 993, 978, 945, 925, 841, 810, 786, 750, 695. ^{1}H NMR: 1.15 s, 9 H (H-15); 1.29 ddd, 1 H, *J*(4,4′) = 12.6, *J*(4,3) = 12.1, *J*(4,5) = 11.3 (H-4); 1.38 s, 3 H (H-13); 1.41 s, 3 H (H-13′); 1.99 ddd, 1 H, *J*(4,4′) = 12.6, *J*(4′,5) = 2.5, *J*(4′,3) = 2.2 (H-4′); 2.40 dd, 1 H, *J*(2,2′) = 15.4, *J*(2,3) = 5.5 (H-2); 2.56 dd, 1 H, *J*(2,2′) = 15.4, *J*(2′,3) = 7.1 (H-2′); 2.74 dt, 1 H, *J*(6,7) = 7.4, *J*(6,7′) = *J*(6,5) = 4.7 (H-6); 2.85 dd, 1 H, *J*(7,7′) = 13.5, *J*(7,6) = 7.4 (H-7); 3.05 dd, 1 H, *J*(7,7′) = 13.5, *J*(7′,6) = 4.7 (H-7′); 3.68 s, 3 H (OCH_3); 3.69 ddd, 1 H, *J*(5,4) = 11.3, *J*(5,6) = 4.7, *J*(5,4′) = 2.5 (H-5); 4.22 dddd, 1 H, *J*(3,4) = 12.1, *J*(3,2′) = 7.1, *J*(3,2) = 5.5, *J*(3,4′) = 2.2 (H-3); 7.19–7.32 m, 5 H (H-9, H-10, H-11). ^{13}C NMR: 19.73 (C-13), 29.96 (C-13′), 31.49 (C-15), 34.08 (C-4), 39.07 (C-7), 41.31 (C-2), 43.42 (C-14), 49.27 (C-6), 51.61 (OCH_3), 66.24 (C-3), 70.89 (C-5), 99.09 (C-12), 126.11 (C-10), 127.75 (C-9), 130.42 (C-11), 139.21 (C-8), 171.36 (COOMe). MS (70 eV, *m/z* (rel.%)): 380 (9) [M^+], 365 (2) [$M^+ - CH_3$], 309 (4) [$365^+ - C_4H_8$], 187 (57) [$C_9H_{15}O_3^+$], 175 (10), 169 (15), 155 (4), 137 (6), 129 (100) [$187^+ - CH_3COCH_3$], 101 (16), 97 (24), 91 (22) [$C_7H_7^+$], 59 (31), 57 (30) [$C_4H_9^+$], 43 (14), 41 (13). HRMS $C_{21}H_{32}O_4S$ (M^+) calculated: 380.2021; found: 380.2023.

Methyl (4S,6R)-(+)-6-[(1S)-(tert-butylsulfanyl)-2-(2,4-dichlorophenyl)ethyl]-2,2-dimethyl-1,3-dioxane-4-acetate ((*S,S,R*)-**17j**): 0.48 g (67%) yield from dihydroxyester **11j** after column chromatography (silica gel, light petroleum/diethyl ether, 4:1) following procedure IX; R_F 0.85 (light petroleum/diethyl ether, 2:1); m.p. 90 °C (pentane); $[\alpha]_D^{20}$ +8.8 (*c* 0.74, CH_2Cl_2); de > 96%, determined by NMR; ee = 94%, determined by ^{1}H NMR with (–)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethan-1-ol as chiral cosolvent (6 equiv.). IR (film): 3069, 3039, 2993, 2981, 2969, 2949, 2935, 2866, 1742 (COOMe), 1655, 1637, 1587, 1559, 1474, 1439, 1381, 1365, 1320, 1263, 1251, 1232, 1198, 1168, 1148, 1126, 1095, 1070, 1051, 1039, 999, 975, 941, 887, 875, 845, 743 (m). ^{1}H NMR: 1.01 s, 9 H (H-17); 1.37 s, 3 H (H-15); 1.44 s, 3 H (H-15′); 1.44 ddd, 1 H, *J*(4,4′) = 12.5, *J*(4,5) = 11.6, *J*(4,3) = 11.5 (H-4); 1.88 ddd, 1 H, *J*(4,4′) = 12.5, *J*(4′,5) = 2.4, *J*(4′,3) = 2.1 (H-4′); 2.43 dd, 1 H, *J*(2,2′) = 15.6, *J*(2,3) = 5.8 (H-2); 2.53 dd, 1 H, *J*(7,7′) = 13.7, *J*(7,6) = 10.4 (H-7); 2.58 dd, 1 H, *J*(2,2′) = 15.6, *J*(2′,3) = 7.0 (H-2′); 2.80 ddd, 1 H, *J*(6,7) = 10.4, *J*(6,5) = 5.5, *J*(6,7′) = 4.0 (H-6); 3.34 dd, 1 H, *J*(7,7′) = 13.7, *J*(7′,6) = 4.0 (H-7′); 3.70 s, 3 H (OCH_3); 3.93 ddd, 1 H, *J*(5,4) = 11.6, *J*(5,6) = 5.5, *J*(5,4′) = 2.4 (H-5); 4.31 dddd, 1 H, *J*(3,4) = 11.5, *J*(3,2′) = 7.0, *J*(3,2) = 5.8, *J*(3,4′) = 2.1 (H-3); 7.16 dd, 1 H, *J*(12,13) = 8.2, *J*(12,10) = 2.2 (H-12); 7.27 d, 1 H, *J*(13,12) = 8.2 (H-13); 7.33 d, 1 H, *J*(12,10) = 2.2 (H-10). ^{13}C NMR: 19.66 (C-15), 29.81 (C-15′), 31.24 (C-16), 33.80 (C-4), 36.04 (C-7), 41.27 (C-2), 43.25 (C-16), 46.92 (C-6), 51.67 (OCH_3), 66.17 (C-3), 73.16 (C-5), 99.14 (C-14), 126.35

(C-12), 128.84 (C-13), 132.65 (C-11), 134.30 (C-10), 135.04 (C-9), 136.23 (C-8), 171.47 (C-1). MS (70 eV, *m/z* (rel.%): 448 (0.4) [M^+], 413 (12) [M^+ – Cl], 359 (1) [M^+ – $SC(CH_3)_3$], 317 (2) [359^+ – $H_2C{=}C{=}O$], 281 (12), 187 (26) [$C_9H_{15}O_4^+$], 169 (11) [187^+ – H_2O], 159 (8) [$C_7H_5Cl_2^+$], 129 (100) [187^+ – CH_3COCH_3], 101 (17), 97 (24), 59 (36), 57 (42) [$C_4H_9^+$], 43 (16), 41 (17). For $C_{21}H_{30}Cl_2O_4S$ (449.4) calculated: 56.12% C, 6.73% H; found: 56.46% C, 6.88% H.

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