Asymmetric Synthesis of 4′-Quaternary 2′-Deoxy-3′- and -4′-*epi*-β-*C*- and -*N*-Nucleosides

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Abstract: A versatile and efficient route to both enantiomers of 4′-quaternary 2′-deoxy-3′- and -4′-*epi*-β-*C*- and -*N*-nucleosides is described. The asymmetric synthesis involves the SAMP/RAMP-hydrazone α-alkylation methodology and diastereoselective nucleophilic 1,2-additions. Manipulation of the substituents in the anomeric position leads to the thermodynamically more stable β-anomers of excellent diastereo- and enantiomeric purity (>99% de and ee).

Key words: nucleoside analogues, asymmetric synthesis, hydrazones, quaternary stereocentres, diastereoselective reduction

A great number of nucleoside analogues have been synthesised and studied recently. Among them, *C*- as well as *N*-nucleosides have been investigated with regard to their biological activity,[1] their behaviour in oligonucleotides,[2] and their ability to replace their natural archetypes,[3] with many of them showing promising bioactivity.

A variety of nucleoside analogues have been synthesised, with modifications of the sugar moiety[4] as well as of the aglyconic unit.[3,5–7] To our knowledge, no asymmetric and direct route to 4′-quaternary 2′-deoxy-3′/4′-*epi*-nucleosides (Figure 1) has been published so far, although nucleosides close to these targets have been investigated and reported. For example, Matsuda et al.[1a] studied the biological activities of 4′-quaternary thymidines and found that some of them possess antileukaemic and antiviral activity. The investigations of Marx et al. on the same analogues with DNA polymerases proved the methyl-substituted thymidine to be superior to the natural thymidines concerning efficiency as well as selectivity.[2] Moreover, Naegli et al. inserted 4′-*epi*-nucleoside analogues in DNA templates and showed them to have the potential to stop DNA polymerases, which could be useful in anticancer drug targeting.[8]

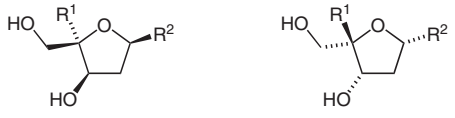

Figure 1 4′-Quaternary 2′-deoxy-3′- and -4′-*epi*-β-nucleosides

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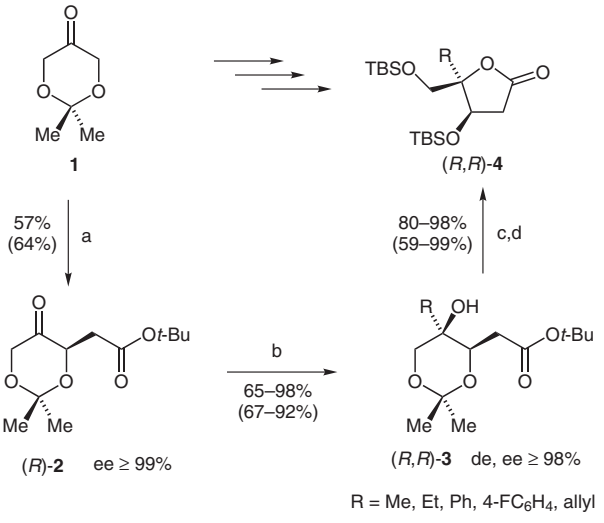
In connection with these investigations, we envisaged to develop an asymmetric synthesis of 4′-quaternary *C*- as well as *N*-nucleoside analogues. We now wish to disclose our results in detail, partially based on a recent communication.[9]

The syntheses of both the *C*- and *N*-nucleoside analogues involve the TBS-protected lactone intermediates **4**, which could be obtained by a six-step reaction sequence (Scheme 1). Starting with the α-alkylation of 2,2-dimethyl-1,3-dioxan-5-one (**1**),[10] the use of the SAMP/RAMP-hydrazone methodology[11] yielded the *tert*-butyl keto esters (*R*)-**2** (via RAMP) and (*S*)-**2** (via SAMP) in 57% and 64% yield, respectively, over three steps with virtually complete asymmetric inductions (≥99% ee). The diastereoselectivity of the subsequent Grignard addition reaction with alkyl and aryl groups was good to excellent (70–98%) and the major *syn*-diastereomers could be separated easily by column chromatography, leading to diastereo- and enantiomerically pure hydroxy esters **3a–e** in 65–98% yields (≥99% de and ee) (Scheme 1, Table 1).

Hydroxy esters **3** were subjected to acidic acetonide cleavage and cyclisation in hydrochloric acid–methanol (Scheme 1), and this gave access to the corresponding lactone diols in excellent yields, with all stereocentres kept intact. The lactone intermediates **5a–e** could be recrystal-



Scheme 1 *Reagents and conditions*: (a) 1. RAMP (or SAMP), benzene, reflux; 2. *t*-BuLi, THF, –78 °C; 3. O_3, CH_2Cl_2, –78 °C; (b) 1. RMgBr, THF, –78 °C or –100 °C; 2. column chromatography; (c) 3 N HCl, MeOH, r.t.; (d) TBSOTf, py, THF, 0 °C. (Yields in brackets are those of the enantiomeric series based on the SAMP auxiliary.)

Table 1 Synthesis of TBS-Protected Lactones **4a–e**

R	3	Yield (%)		de,[a] ee[b] (%)	4	Yield (%)	
		(*R*,*R*)-**3**	(*S*,*S*)-**3**	of **3**		(*R*,*R*)-**4**	(*S*,*S*)-**4**
Me	**3a**	87	89	≥99, ≥99	**4a**	85	88
Et	**3b**	66	75	≥99, ≥99	**4b**	98	59
Ph	**3c**	88	92	≥99, ≥99	**4c**	89	99
4-FC_6H_4	**3d**	98	67	≥99, ≥99	**4d**	80	74
allyl	**3e**	66	80	≥99, ≥99	**4e**	90	74

[a] Determined by GC (CP-Sil-8) after column chromatography.
[b] Determined by CSP-GC (Chiral-dex, Chirasil L-Val).

lised from tetrahydrofuran–*n*-pentane. For lactone **5b** (R = Et), we were able to perform an X-ray crystal structure analysis to determine the absolute configuration (Figure 2).

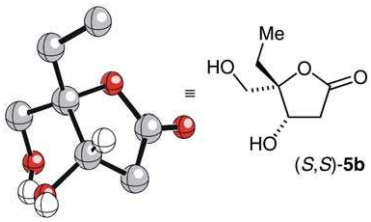
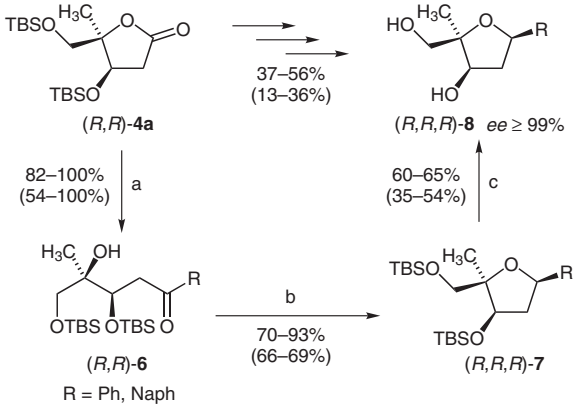


Figure 2 Structure of (*S*,*S*)-**5b** as determined by X-ray crystallography[12]

For the ongoing synthesis, however, most lactone diols were directly protected by reaction with *tert*-butyldimethylsilyl trifluoromethanesulfonate and pyridine to give the doubly TBS-protected lactones **4a–e** in good to excellent yields (Scheme 1, Table 1).

For the preparation of *C*-nucleosides, lactone **4a** was treated with freshly prepared organocerium reagents[13] to give the open doubly protected keto triol **6** in good to quantitative yields (Scheme 2). Subsequent reduction of **6** with tetramethylammonium triacetoxyborohydride[14] gave rise exclusively to β-anomers **7** of the protected nucleosides in good to very good yields (Scheme 2, Table 2). Finally, deprotection of **7** could be achieved by treatment of **7** with trifluoroacetic acid in chloroform; this gave free *C*-nucleosides **8** (Scheme 2). The enantiomeric excess (≥99% ee) was maintained throughout the synthesis, and could be verified in the final products **8a**,**b** (Table 2).

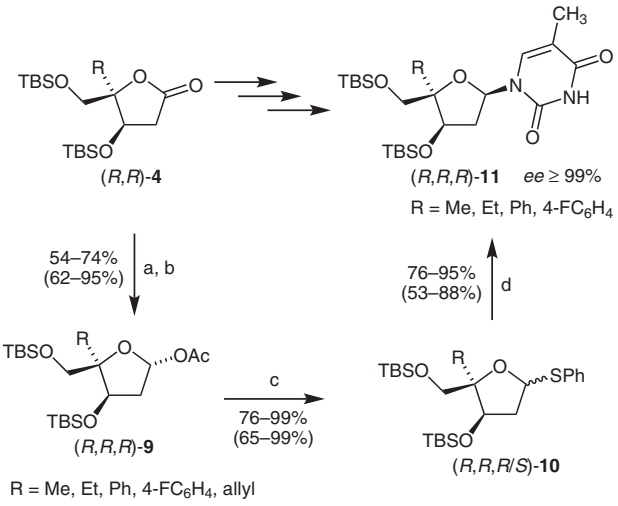
The synthesis of *N*-nucleosides first required the reduction of the TBS-protected lactones **4a–e** (Scheme 3). This



Scheme 2 *Reagents and conditions*: (a) $CeCl_3$, RLi, THF, –110 to –99 °C; (b) $Me_4N^+[HB(OAc)_3]^-$, MeCN, AcOH, –30 °C; (c) TFA–$CHCl_3$ (4:1), $CHCl_3$, 0 °C. [Yields in brackets are those of the opposite enantiomeric series, starting from (*S*,*S*)-**4a**.]

was achieved with diisobutylaluminum hydride, resulting in the corresponding lactols, which were acylated without preliminary purification to lead to lactol esters **9a–e** in yields ranging from 54% to 95% (Scheme 3, Table 3). It is noteworthy that under these reduction conditions the α-anomers formed exclusively.

Outright substitution with silylated bases by the Vorbrüggen methodology[5] failed, and therefore lactol esters **9** were exposed to nucleophilic substitution with trimethyl(phenylsulfanyl)silane,[15] which led to an anomeric mixture of thioglycosides **10a–e** (Scheme 3). These



Scheme 3 *Reagents and conditions*: (a) DIBAL-H, CH_2Cl_2, –78 °C; (b) Ac_2O, py, r.t.; (c) TMSSPh, $BF_3{\cdot}OEt_2$, *n*-hexane, –95 °C to r.t.; (d) bis-TMS-thymine, NBS, 4-Å MS, CH_2Cl_2, –78 to –26 °C. [Yields in brackets are those of the opposite enantiomeric series, starting from (*S*,*S*)-**4**.]

Table 2 Preparation of *C*-Nucleosides **8a**,**b**

R	6	Yield (%)		7	Yield (%)		8	Yield (%)	
		(*R*,*R*)-**6**	(*S*,*S*)-**6**		(*R*,*R*,*R*)-**7**	(*S*,*S*,*S*)-**7**		(*R*,*R*,*R*)-**8**	(*S*,*S*,*S*)-**8**
Ph	**6a**	82	54	**7a**	70	69	**8a**	65	35
1-Naph	**6b**	100	100	**7b**	93	66	**8b**	60	54

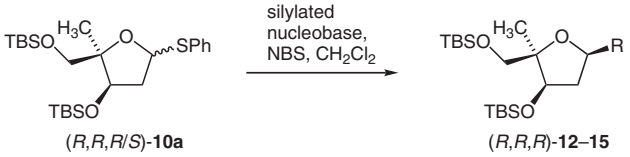
Table 3 Synthesis of Protected *N*-Nucleosides **11a–e**

R	**9**	Yield (%)		**10**	Yield (%)		**11**	Yield (%)	
		(*R*,*R*,*R*)-**9**	(*S*,*S*,*S*)-**9**		(*R*,*R*,*R*)-**10**	(*S*,*S*,*S*)-**10**		(*R*,*R*,*R*)-**11**	(*S*,*S*,*S*)-**11**
Me	**9a**	54	74	**10a**	98	86	**11a**	77	77
Et	**9b**	54	62	**10b**	97	99	**11b**	95	88
Ph	**9c**	62	95	**10c**	89	98	**11c**	87	73
4-FC_6H_4	**9d**	74	64	**10d**	99	65	**11d**	76	53
allyl	**9e**	64	74	**10e**	76	68	**11e**	–[a]	–[a]

[a] Derivatives **11e** were unstable and could not be purified.

intermediates turned out to be excellent substrates for the *N*-bromosuccinimide-activated silyl-Hilbert–Johnson reaction[16] to give the thermodynamically more stable β-anomers of thymidines **11a–d** in high diastereoselectivity and good to excellent yields (Scheme 3, Table 3). Only the allyl derivatives **11e** turned out to be unstable and could not be purified (Table 3).

The deprotection of thymidine (*S*,*S*,*S*)-**11a** was performed as in the case of the *C*-nucleosides with trifluoroacetic acid in chloroform, and gave the unprotected nucleoside analogue in 66% yield. Moreover, further nucleobases were attached to **10a** by use of *N*-bromosuccinimide and the corresponding silylated heterocycles in dichloromethane; this led to the formation of 4′-methyl-2′-deoxy-3′- and -4′-*epi*-β-*N*-nucleosides **12–15** (Scheme 4, Table 4).



Scheme 4 Introduction of other nucleobases onto **10a**

Table 4 Preparation of Further Nucleoside Analogues from **10a**

R	Product	Yield (%) (*R*,*R*,*R*)	Yield (%) (*S*,*S*,*S*)
cytosine	**12**	48	50
N-Ac-guanine	**13**	37	46
xanthine	**14**	42	76
6-chloropurine	**15**	35 (α) + 42 (β)	28 (α) + 55 (β)

In contrast to all the other cases, the reaction with silylated adenine gave only poor results (15% and 16% yield). For this reason we decided to introduce the less polar adenine precursor 6-chloropurine into the system, which could be transformed into adenine by amination in an additional step. This provided an access to the desired nucleoside analogues **15**. Exclusively in this case, a considerable amount of the α-anomer was found in the reaction mixture (Table 4). The diastereomers could be separated easily by column chromatography and were obtained in 77% and 83% combined yields.

In summary, we have demonstrated an efficient and flexible synthetic route towards diastereomerically and enantiomerically pure 4′-quaternary 3′- and -4′-*epi*-*C*- and -*N*-nucleosides. The free *C*-nucleosides **8a**,**b** were synthesised in nine steps and overall yields of 7–24%. TBS-protected *N*-nucleosides **11a–d** and **12–15** were prepared in 8–34% overall yield, following a ten-step synthetic sequence.

All chemicals were purchased from commercial sources and used without further treatment unless otherwise indicated. Solvents were dried by standard procedures, and reactions requiring anhydrous conditions were performed under argon. All melting points were measured on a Büchi 510 (Dr. Tottoli system) melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer P241 polarimeter. NMR spectra were recorded on a Varian VXR 300, Varian Gemini 300, Varian Inova 400, or Varian Unity 500 spectrometer; TMS was used as an internal standard. IR spectra were recorded on a Perkin-Elmer FT/IR 1760 spectrometer. MS spectra were measured on a Finnigan SSQ7000, and HRMS spectra on a Finnigan MAT95 mass spectrometer. Elemental analyses were obtained with a Heraeus CHN-O-Rapid analyser. For preparative column chromatography, silica gel 60 (particle size 0.040–0.063 mm, Merck) was used. For analytical TLC, pre-coated F_{254} silica gel 60 plates (Merck, Darmstadt) were used.

Hydroxy Esters 3a–d; General Procedure (GP1)

The Grignard reagent RMgBr (2 equiv) was slowly added to a 0.1 M soln of keto ester **2** in anhyd THF at –100 °C (–78 °C for R = Me). After 4 h, the reaction was stopped by the addition of sat. aq NH_4Cl (5 mL/mmol). After the mixture had warmed to r.t., the precipitate was dissolved by dilution with distilled H_2O. The aqueous phase was extracted with Et_2O (50 mL/mmol) and the combined organic layers were washed with brine and dried ($MgSO_4$). The products were purified by column chromatography.

(4*S*,5*S*)-*tert*-Butyl 2-(5-Hydroxy-2,2,5-trimethyl-1,3-dioxan-4-yl)acetate [(*S*,*S*)-3a]

According to GP1, keto ester (*S*)-**2** (1.247 g, 5.10 mmol) was treated with MeMgBr at –78 °C. After workup and column chromatography (*n*-pentane–Et_2O, 1:1), hydroxy ester (*S*,*S*)-**3a** was obtained as colourless crystals.

Yield: 1.164 g (88%); mp 67 °C; $[\alpha]_D^{25}$ –9.8 (*c* 1.10, $CHCl_3$); R_f = 0.1 (*n*-pentane–Et_2O, 4:1).

IR (KBr): 3559, 3495, 2981, 2941, 1724, 1384, 1369, 1311, 1288, 1263, 1205, 1151, 1062, 1038, 968 cm^{-1}.

^1H NMR (300 MHz, C_6D_6): δ = 0.69 (s, 3 H, CH_3COH), 1.25 (s, 3 H, CH_3CCH_3), 1.34 (s, 3 H, CH_3CCH_3), 1.37 [s, 9 H, $C(CH_3)_3$], 2.50 (dd, *J* = 15.8, 4.0 Hz, 1 H, CH_2CO), 2.62 (dd, *J* = 15.8, 8.7 Hz, 1 H, CH_2CO), 2.92 (s, 1 H, OH), 3.30 (d, *J* = 11.8 Hz, 1 H, CH_2O), 3.41 (d, *J* = 11.8 Hz, 1 H, CH_2O), 4.15 (dd, *J* = 8.7, 4.0 Hz, 1 H, CH_2CHO).

^{13}C NMR (75 MHz, C_6D_6): δ = 18.4, 18.9, 28.1, 29.7, 36.1, 66.3, 70.3, 73.8, 79.9, 98.7, 170.3.

MS (CI): *m*/*z* (%) = 261 (3) [M + H^+].

Anal. Calcd for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 60.38; H, 9.64.

(4*R*,5*R*)-*tert*-Butyl 2-(5-Hydroxy-2,2,5-trimethyl-1,3-dioxan-4-yl)acetate [(*R*,*R*)-3a]

According to GP1, keto ester (*R*)-**2** (1.221 g, 5.00 mmol) was treated with MeMgBr at –78 °C. After workup and column chromatography (*n*-pentane–Et_2O, 1:1), hydroxy ester (*R*,*R*)-**3a** was obtained as colourless crystals.

Yield: 1.127 g (87%); $[\alpha]_D^{25}$ +10.2 (*c* 0.94, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**3a**.

(4*S*,5*S*)-*tert*-Butyl 2-(5-Ethyl-5-hydroxy-2,2-dimethyl-1,3-dioxan-4-yl)acetate [(*S*,*S*)-3b]

According to GP1, keto ester (*S*)-**2** (0.122 g, 0.50 mmol) was treated with EtMgBr at –100 °C. After workup and column chromatography (*n*-pentane–Et_2O, 4:1) (*S*,*S*)-**3b** was obtained as colourless crystals.

Yield: 0.104 g (75%); mp 47 °C; $[\alpha]_D^{25}$ –11.0 (*c* 1.00, $CHCl_3$); R_f = 0.3 (*n*-pentane–Et_2O, 2:1).

IR (KBr): 3452, 2985, 2949, 2875, 1715, 1473, 1369, 1329, 1295, 1253, 1203, 1164, 1114, 1091, 1072, 1053, 1038, 1003, 980, 946, 906, 866, 832, 587, 537, 519 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.6 Hz, 3 H, CH_3CH_2), 1.40 (s, 3 H, CH_3CCH_3), 1.44 [s, 9 H, $C(CH_3)_3$], 1.46 (s, 3 H, CH_3CCH_3), 2.39 (dd, *J* = 15.6, 8.8 Hz, 1 H, CH_2CO), 2.50 (dd, *J* = 15.6, 3.8 Hz, 1 H, CH_2CO), 3.06 (s, 1 H, OH), 3.58 (d, *J* = 11.9 Hz, 1 H, CH_2O), 3.85 (d, *J* = 11.9 Hz, 1 H, CH_2O), 4.22 (dd, *J* = 8.8, 3.8 Hz, 1 H, CH_2CHO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 6.9, 18.3, 25.9, 28.1, 29.4, 35.8, 67.8, 68.2, 72.8, 80.4, 98.8, 170.9.

MS (CI): *m*/*z* (%) = 275 (9) [M + H^+].

Anal. Calcd for $C_{14}H_{26}O_5$: C, 61.29; H, 9.55. Found: C, 61.17; H, 9.94.

(4*R*,5*R*)-*tert*-Butyl 2-(5-Ethyl-5-hydroxy-2,2-dimethyl-1,3-dioxan-4-yl)acetate [(*R*,*R*)-3b]

According to GP1, keto ester (*R*)-**2** (0.222 g, 0.91 mmol) was treated with EtMgBr at –100 °C. After workup and column chromatography (*n*-pentane–Et_2O, 4:1), (*R*,*R*)-**3b** was obtained as colourless crystals.

Yield: 0.164 g (66%); $[\alpha]_D^{25}$ +11.2 (*c* 1.05, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**3b**.

(4*S*,5*S*)-*tert*-Butyl 2-(5-Hydroxy-2,2-dimethyl-5-phenyl-1,3-dioxan-4-yl)acetate [(*S*,*S*)-3c]

According to GP1, keto ester (*S*)-**2** (0.122 g, 0.50 mmol) was treated with PhMgBr at –100 °C. After workup and column chromatography (*n*-pentane–Et_2O, 2:1), (*S*,*S*)-**3c** was obtained as colourless crystals.

Yield: 0.149 g (92%); mp 108 °C; $[\alpha]_D^{25}$ +12.2 (*c* 1.00, $CHCl_3$); R_f = 0.51 (*n*-pentane–Et_2O, 2:1).

IR (KBr): 3449, 2989, 2921, 1727, 1494, 1450, 1406, 1384, 1371, 1307, 1284, 1256, 1198, 1164, 1092, 1075, 1030, 978, 949, 936, 900, 859, 829, 765, 746, 706 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.37 [s, 9 H, $C(CH_3)_3$], 1.50 (s, 3 H, CH_3CCH_3), 1.63 (s, 3 H, CH_3CCH_3), 2.08 (dd, *J* = 15.9, 2.8 Hz, 1 H, CH_2CO), 2.41 (dd, *J* = 15.9, 9.6 Hz, 1 H, CH_2CO), 3.48 (s, 1 H, OH), 3.57 (d, *J* = 12.0 Hz, 1 H, CH_2O), 4.20 (d, *J* = 12.0 Hz, 1 H, CH_2O), 4.67 (dd, *J* = 9.6, 2.8 Hz, 1 H, CH_2CHO), 7.20–7.50 (m, 5 H, *H*Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 28.0, 29.6, 35.8, 70.6, 70.7, 73.3, 80.4, 99.4, 125.2, 127.7, 128.5, 138.7, 170.6.

MS (CI): *m*/*z* (%) = 267 (100), 323 (10) [M + H^+].

Anal. Calcd for $C_{18}H_{26}O_5$: C, 67.06; H, 8.13. Found: C, 66.56; H, 8.62.

(4*R*,5*R*)-*tert*-Butyl 2-(5-Hydroxy-2,2-dimethyl-5-phenyl-1,3-dioxan-4-yl)acetate [(*R*,*R*)-3c]

According to GP1, keto ester (*R*)-**2** (0.279 g, 1.14 mmol) was treated with PhMgBr at –100 °C. After workup and column chromatography (*n*-pentane–Et_2O, 2:1), (*R*,*R*)-**3c** was obtained as colourless crystals.

Yield: 0.323 g (88%); $[\alpha]_D^{25}$ –12.6 (*c* 1.00, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**3c**.

(4*S*,5*S*)-*tert*-Butyl 2-[5-(4-Fluorophenyl)-5-hydroxy-2,2-dimethyl-1,3-dioxan-4-yl]acetate [(*S*,*S*)-3d]

According to GP1, keto ester (*S*)-**2** (0.370 g, 1.51 mmol) was treated with 4-FC_6H_4MgBr at –100 °C. After workup and column chromatography (*n*-pentane–Et_2O, 2:1), (*S*,*S*)-**3d** was obtained as colourless crystals.

Yield: 0.345 g (67%); mp 112 °C; $[\alpha]_D^{25}$ +11.8 (*c* 0.98, $CHCl_3$); R_f = 0.6 (*n*-pentane–Et_2O, 2:1).

IR (KBr): 3432, 2985, 2927, 2868, 1713, 1605, 1513, 1384, 1369, 1332, 1310, 1280, 1256, 1226, 1192, 1157, 1130, 1085, 1036, 983, 959, 936, 907, 867, 830, 748, 597, 560, 539 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.38 [s, 9 H, $C(CH_3)_3$], 1.50 (s, 3 H, CH_3CCH_3), 1.64 (s, 3 H, CH_3CCH_3), 2.08 (dd, *J* = 16.1, 3.0 Hz, 1 H, CH_2CO), 2.41 (dd, *J* = 16.1, 9.4 Hz, 1 H, CH_2CO), 3.55 (d, *J* = 12.1 Hz, 1 H, CH_2O), 3.68 (s, 1 H, OH), 4.17 (d, *J* = 12.1 Hz, 1 H, CH_2O), 4.67 (dd, *J* = 9.4, 3.0 Hz, 1 H, CH_2CHO), 7.05 (dd, *J* = 8.9, 8.7 Hz, 2 H, FCC*H*), 7.50 (dd, *J* = 8.9, 8.7 Hz, 2 H, CC*H*CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.3, 28.0, 29.4, 35.7, 70.4, 70.4, 73.1, 80.3, 99.3, 115.2 (d, J_{C-F} = 20.6 Hz, 2 C, FC*C*H), 126.9 (d, J_{C-F} = 7.6 Hz, 2 C, C*C*HCH), 134.5 (d, J_{C-F} = 3.1 Hz, 1 C, *C*COH), 162.0 (d, J_{C-F} = 246.4 Hz, 1 C, *C*F), 170.3.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –114.72.

MS (CI): *m*/*z* (%) = 209 (100), 285 (20).

Anal. Calcd for $C_{18}H_{25}FO_5$: C, 63.51; H, 7.40. Found: C, 63.28; H, 7.91.

(4*R*,5*R*)-*tert*-Butyl 2-[5-(4-Fluorophenyl)-5-hydroxy-2,2-dimethyl-1,3-dioxan-4-yl]acetate [(*R*,*R*)-3d]

According to GP1, keto ester (*R*)-**2** (0.270 g, 1.11 mmol) was treated with 4-FC_6H_4MgBr at –100 °C. After workup and column chromatography (*n*-pentane–Et_2O, 2:1), (*R*,*R*)-**3d** was obtained as colourless crystals.

Yield: 0.369 g (98%); $[\alpha]_D^{25}$ –9.6 (*c* 0.99, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**3d**.

(4*S*,5*S*)-*tert*-Butyl 2-(5-Allyl-5-hydroxy-2,2-dimethyl-1,3-dioxan-4-yl)acetate [(*S*,*S*)-3e]

$ZnBr_2$ (0.137 g, 0.60 mmol, 1.2 equiv) was dried under vacuum and dissolved in anhyd THF (5 mL/mmol) and the mixture was cooled to –78 °C. AllMgBr (0.6 mL, 0.6 mmol, 1.2 equiv) was added slowly and the mixture was allowed to stir for 30 min. It was then cooled to –100 °C and (*S*)-**2** (0.122 g, 0.50 mmol, 1.0 equiv) in anhyd THF (5 mL/mmol) was added. After 1 h, the reaction was quenched by the addition of H_2O (10 mL/mmol). After workup as described in GP1 and column chromatography (*n*-pentane–Et_2O, 1:1), (*S*,*S*)-**3e** was obtained as colourless crystals.

Yield: 0.114 g (80%); mp 49 °C; $[\alpha]_D^{25}$ 0 (*c* 1.00, $CHCl_3$); R_f = 0.6 (*n*-pentane–Et_2O, 1:1).

IR (KBr): 3439, 2981, 2936, 2874, 1715, 1641, 1370, 1314, 1280, 1258, 1204, 1158, 1088, 1063, 1030, 973, 955, 909, 883, 831, 752, 739, 620, 585, 529 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.40 (s, 3 H, CH_3CCH_3), 1.45 [br, 12 H, CH_3CCH_3, $C(CH_3)_3$], 2.07 (ddd, *J* = 14.4, 8.2, 1.0 Hz, 1 H, CH_2COH), 2.22 (ddd, *J* = 14.4, 6.7, 1.2 Hz, 1 H, CH_2COH), 2.41 (dd, *J* = 15.6, 8.9 Hz, 1 H, CH_2CO), 2.54 (dd, *J* = 15.6, 3.7 Hz, 1 H, CH_2CO), 3.07 (d, *J* = 1.2 Hz, 1 H, OH), 3.52 (d, *J* = 11.9 Hz, 1 H, CH_2O), 3.83 (d, *J* = 11.9 Hz, 1 H,CH_2O), 4.22 (dd, *J* = 8.9, 3.7 Hz, 1 H, CH_2CHO), 5.07–5.14 (m, 2 H, CH_2CHCH_2), 5.75–5.89 (m, 1 H, CH_2CHCH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 28.0, 29.3, 35.8, 38.1, 67.9, 68.3, 72.5, 80.5, 98.9, 118.8, 131.6, 170.7.

MS (CI): *m*/*z* (%) = 231 (100), 287 (8) [M + H^+].

HRMS: *m*/*z* [M – CH_3]$^+$ calcd for $C_{14}H_{23}O_5$: 271.154; found: 271.154.

(4*R*,5*R*)-*tert*-Butyl 2-(5-Allyl-5-hydroxy-2,2-dimethyl-1,3-dioxan-4-yl)acetate [(*R*,*R*)-3e]

$ZnBr_2$ (0.639 g, 2.8 mmol, 1.2 equiv) was dried under vacuum and dissolved in anhyd THF (5 mL/mmol) and the mixture was cooled to –78 °C. AllMgBr (2.8 mL, 2.8 mmol, 1.2 equiv) was added slowly and the mixture was allowed to stir for 30 min. It was then cooled to –100 °C and (*R*)-**2** (0.570 g, 2.33 mmol, 1.0 equiv) in anhyd THF (5 mL/mmol) was added. After 1 h, the reaction was quenched by the addition of H_2O (10 mL/mmol). After workup as described in GP1 and column chromatography (*n*-pentane–Et_2O, 1:1), (*R*,*R*)-**3e** was obtained as colourless crystals.

Yield: 0.437 g (65%); $[\alpha]_D^{25}$ –0.7 (*c* 1.20, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**3e**.

TBS-Protected Lactones 4a–e; General Procedure (GP2)

The appropriate hydroxy ester, one of **3a**–**e**, was dissolved in MeOH (3 mL/mmol) and treated with 3 N HCl in aq MeOH (12 N aq HCl–MeOH, 1:4; 3 mL/mmol). The mixture was stirred until TLC indicated complete conversion of the starting material. All solvents were evaporated under reduced pressure and the products were recrystallised from THF–*n*-pentane. The free lactones (1 equiv) were then dissolved in THF (10 mL/mmol) and py (6 equiv) was added at 0 °C. After slow addition of TBSOTf (3 equiv), the reaction mixture was stirred for 4 h and then quenched with H_2O (5 mL/mmol), extracted with Et_2O (50 mL/mmol), washed with brine, and dried ($MgSO_4$). Column chromatography gave pure products **4a**–**e**.

(4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyldihydrofuran-2(3*H*)-one [(*S*,*S*)-4a]

The hydroxy ester (*S*,*S*)-**3a** (0.573 g, 2.16 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.315 g (99%); mp 80 °C; $[\alpha]_D^{25}$ –2.87 (*c* 1.05, MeOH). The resulting lactone (0.083 g, 0.57 mmol) was treated with TBSOTf and py as described in GP2. The product (*S*,*S*)-**4a** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.195 g (89%); mp 44 °C; $[\alpha]_D^{25}$ +23.9 (*c* 1.15, $CHCl_3$); R_f = 0.4 (*n*-pentane–Et_2O, 4:1).

IR (KBr): 2955, 2932, 2893, 2860, 1777, 1470, 1258, 1230, 1117, 1001, 955, 915, 879, 840, 777, 671 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$), 0.89 [s, 9 H, $C(CH_3)_3$], 0.90 [s, 9 H, $C(CH_3)_3$], 1.30 (s, 3 H, CH_3C), 2.66 (dd, *J* = 17.0, 7.7 Hz, 1 H, CH_2CO), 2.75 (dd, *J* = 17.0, 7.7 Hz, 1 H, CH_2CO), 3.61 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 3.91 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 4.23 (dd, *J* = 7.7, 7.7 Hz, 1 H, $CHCH_2CO$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.7, –5.6, –5.2, –4.7, 17.9, 18.2, 21.2, 25.6, 25.8, 39.0, 65.4, 74.5, 87.4, 174.3.

MS (CI): *m*/*z* (%) = 243 (100), 377 (2) [M + H^+].

Anal. Calcd for $C_{18}H_{38}O_4Si$: C, 57.70; H, 10.22. Found: C, 57.55; H, 10.53.

(4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyldihydrofuran-2(3*H*)-one [(*R*,*R*)-4a]

The hydroxy ester (*R*,*R*)-**3a** (0.825 g, 3.38 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.493 g (99%); $[\alpha]_D^{23}$ +2.96 (*c* 1.02, MeOH).

The resulting lactone (0.157 g, 1.08 mmol) was treated with TBSOTf and py as described in GP2. The product (*R*,*R*)-**4a** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.345 g (86%); $[\alpha]_D^{25}$ –24.0 (*c* 1.02, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**4a**.

(4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-ethyldihydrofuran-2(3*H*)-one [(*S*,*S*)-4b]

The hydroxy ester (*S*,*S*)-**3b** (0.137 g, 0.50 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.079 g (99%); mp 112 °C; $[\alpha]_D^{25}$ +5.7 (*c* 1.04, MeOH).

The resulting lactone (0.061 g, 0.38 mmol) was treated with TBSOTf and py as described in GP2. The product (*S*,*S*)-**4b** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.088 g (60%); mp 43 °C; $[\alpha]_D^{25}$ +22.6 (*c* 0.97, $CHCl_3$); R_f = 0.8 (*n*-pentane–Et_2O, 2:1).

IR (KBr): 2954, 2933, 2891, 2859, 1763, 1468, 1256, 1227, 1171, 1103, 1079, 1037, 1004, 926, 843, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.06–0.09 (4 s, 12 H, $SiCH_3$), 0.89–0.90 [2 s, 18 H, $C(CH_3)_3$], 0.95 (t, *J* = 7.4 Hz, 3 H, CH_3CH_2), 1.64 (q, *J* = 7.4 Hz, 2 H, CH_3CH_2), 2.66 (dd, *J* = 17.0, 8.2 Hz, 1 H, CH_2CO), 2.78 (dd, *J* = 17.0, 8.2 Hz, 1 H, CH_2CO), 3.65 (d, *J* = 10.7 Hz, 1 H, CH_2OSi), 3.95 (d, *J* = 10.7 Hz, 1 H, CH_2OSi), 4.32 (dd, *J* = 8.2, 8.2 Hz, 1H, H-3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.7, –5.6, –5.2, –4.5, 7.6, 17.9, 18.2, 25.6, 25.8, 26.9, 39.1, 64.0, 71.9, 89.4, 174.2.

MS (CI): *m*/*z* (%) = 331 (100), 390 (6) [M + H^+].

HRMS: *m*/*z* [M – C_4H_9]$^+$ calcd for $C_{15}H_{31}O_4Si_2$: 331.176; found: 331.176.

(4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-ethyldihydrofuran-2(3*H*)-one [(*R*,*R*)-4b]

The hydroxy ester (*R*,*R*)-**3b** (0.164 g, 0.60 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.095 g (99%); $[\alpha]_D^{25}$ –7.16 (*c* 1.02, MeOH).

The resulting lactone (0.108 g, 0.67 mmol) was treated with TBSOTf and py as described in GP2. The product (*R*,*R*)-**4b** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.258 g (99%); $[\alpha]_D^{25}$ –18.0 (*c* 0.99, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**4b**.

(4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-phenyldihydrofuran-2(3*H*)-one [(*S*,*S*)-4c]

The hydroxy ester (*S*,*S*)-**3c** (0.156 g, 0.49 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.101 g (99%); mp 125 °C; $[\alpha]_D^{25}$ –6.9 (*c* 0.95, MeOH).

The resulting lactone (0.110 g, 0.53 mmol) was treated with TBSOTf and py as described in GP2. The product (*S*,*S*)-**4c** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.232 g (100%); mp 61 °C; $[\alpha]_D^{25}$ +13.4 (*c* 0.83, $CHCl_3$); R_f = 0.7 (*n*-pentane–Et_2O, 4:1).

IR (KBr): 2953, 2933, 2890, 2859, 1791, 1468, 1402, 1256, 1136, 1112, 1026, 938, 839, 781, 756, 705 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.00–0.02 (2 s, 6 H, $SiCH_3$), 0.09–0.11 (2s, 6 H, $SiCH_3$), 0.87 [s, 9 H, $C(CH_3)_3$], 0.97 [s, 9 H, $C(CH_3)_3$], 2.66 (dd, *J* = 16.8, 7.9 Hz, 1 H, CH_2CO), 2.88 (dd, *J* = 16.8, 7.9 Hz, 1 H, CH_2CO), 3.75 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 4.26 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 4.53–4.58 (dd, *J* = 7.9, 7.9 Hz, 1 H, $CHCH_2CO$), 7.31–7.47 (m, 5 H, *H*Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.8, –5.7, –5.1, –4.3, 17.9, 18.2, 25.7, 25.8, 39.0, 66.1, 75.0, 89.8, 124.5, 128.0, 128.4, 140.0, 173.9.

MS (CI): *m*/*z* (%) = 203 (100), 437 (17) [M + H^+].

Anal. Calcd for $C_{23}H_{40}O_4Si_2$: C, 63.25; H, 9.23. Found: C, 63.51; H, 9.29.

(4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-phenyldihydrofuran-2(3*H*)-one [(*R*,*R*)-4c]

The hydroxy ester (*R*,*R*)-**3c** (0.324 g, 1.00 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.208 g (99%); $[\alpha]_D^{24}$ +9.6 (*c* 0.99, MeOH).

The resulting lactone (0.210 g, 1.00 mmol) was treated with TBSOTf and py as described in GP2. The product (*R*,*R*)-**4c** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.390 g (89%); $[\alpha]_D^{25}$ –9.1 (*c* 0.98, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**4c**.

(4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-(4-fluorophenyl)dihydrofuran-2(3*H*)-one [(*S*,*S*)-4d]

The hydroxy ester (*S*,*S*)-**3d** (0.188 g, 0.55 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.124 g (99%); mp 140 °C; $[\alpha]_D^{25}$ –5.9 (*c* 0.97, MeOH).

The resulting lactone (0.104 g, 0.46 mmol) was treated with TBSOTf and py as described in GP2. The product (*S*,*S*)-**4d** could be obtained after column chromatography (*n*-pentane–Et_2O, 6:1) as colourless crystals.

Yield: 0.155 g (74%); mp 90 °C; $[\alpha]_D^{25}$ +9.64 (*c* 0.98, $CHCl_3$); R_f = 0.6 (*n*-pentane–Et_2O, 6:1).

IR (KBr): 2954, 2933, 2891, 2858, 1781, 1511, 1469, 1254, 1226, 1177, 1133, 1082, 950, 929, 841, 779 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$), 0.87 [s, 9 H, $C(CH_3)_3$], 0.96 [s, 9 H, $C(CH_3)_3$], 2.68 (dd, *J* = 16.8, 7.9 Hz, 1 H, CH_2CO), 2.85 (dd, *J* = 16.8, 7.7 Hz, 1 H, CH_2CO), 3.72 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 4.21 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 4.51 (dd, *J* = 7.7, 7.9 Hz, 1 H, $CHCH_2CO$), 7.04 (m, 2 H, FCC*H*), 7.43 (m, 2 H, CC*H*CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.8, –5.7, –5.1, –4.3, 17.9, 18.2, 25.7, 25.8, 38.9, 66.1, 75.0, 89.4, 115.3 (d, J_{C-F} = 21.6 Hz, 2 C, FC*C*H), 126.4 (d, J_{C-F} = 7.7 Hz, 2 C, C*C*HCH), 135.9 (d, J_{C-F} = 3.0 Hz, *C*CHCH), 162.5 (d, J_{C-F} = 47.2 Hz, 1 C, *C*F), 173.6.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –114.0.

MS (CI): *m*/*z* (%) = 203 (100), 456 (5) [M + H^+].

Anal. Calcd for $C_{23}H_{39}FO_4Si_2$: C, 60.75; H, 8.64. Found: C, 60.77; H, 9.08.

(4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-(4-fluorophenyl)dihydrofuran-2(3*H*)-one [(*R*,*R*)-4d]

The hydroxy ester (*R*,*R*)-**3d** (0.371 g, 1.09 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.245 g (99%); $[\alpha]_D^{23}$ +8.3 (*c* 1.00, MeOH).

The resulting lactone (0.130 g, 0.58 mmol) was treated with TBSOTf and py as described in GP2. The product (*R*,*R*)-**4d** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.214 g (81%); $[\alpha]_D^{23}$ –9.85 (*c* 1.02, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**4d**.

(4*S*,5*S*)-5-Allyl-4-(*tert*-butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]dihydrofuran-2(3*H*)-one [(*S*,*S*)-4e]

The hydroxy ester (*S*,*S*)-**3e** (0.141 g, 0.49 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.084 g (99%); mp 69 °C; $[\alpha]_D^{26}$ +2.8 (*c* 1.00, MeOH).

The resulting lactone (0.067 g, 0.39 mmol) was treated with TBSOTf and py as described in GP2. The product (*S*,*S*)-**4e** could be obtained after column chromatography (*n*-pentane–Et_2O, 10:1) as colourless crystals.

Yield: 0.118 g (75%); mp 47 °C; $[\alpha]_D^{25}$ +11.96 (*c* 1.13, $CHCl_3$); R_f = 0.31 (*n*-pentane–Et_2O, 10:1).

IR (KBr): 2957, 2933, 2896, 2859, 1788, 1469, 1257, 1231, 1134, 1071, 933, 883, 839, 777 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.06 (2s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.89 [s, 9 H, $C(CH_3)_3$], 0.90 [s, 9 H, $C(CH_3)_3$], 2.36 (d, *J* = 7.2 Hz, 2 H, CH_2CHCH_2), 2.65 (dd, *J* = 17.1, 7.9 Hz, 1 H, CH_2CO), 2.75 (dd, *J* = 17.1, 7.9 Hz, 1 H, CH_2CO), 3.62 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 3.94 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 4.35 (dd, *J* = 7.9, 7.9 Hz, 1 H, $CHCH_2CO$), 5.10–5.19 (m, 2 H, CH_2CHCH_2), 5.71–5.82 (m, 1 H, CH_2CHCH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.7, –5.6, –5.1, –4.5, 17.9, 18.2, 25.6, 25.8, 38.4, 38.9, 64.6, 71.6, 88.6, 119.7, 131.6, 174.3 (C-1).

MS (CI): *m*/*z* (%) = 269 (100), 403 (2) [M + H^+].

Anal. Calcd for $C_{20}H_{40}O_4Si_2$: C, 59.95; H, 10.06. Found: C, 59.52; H, 10.13.

(4*R*,5*R*)-5-Allyl-4-(*tert*-butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]dihydrofuran-2(3*H*)-one [(*R*,*R*)-4e]

Hydroxy ester (*R*,*R*)-**3e** (0.437 g, 1.53 mmol) was cyclised according to GP2. Recrystallisation afforded the free lactone as colourless crystals.

Yield: 0.265 g (99%); $[\alpha]_D^{24}$ –2.4 (*c* 1.03, MeOH).

The resulting lactone (0.830 g, 0.48 mmol) was treated with TBSOTf and py as described in GP2. The product (*R*,*R*)-**4e** could be obtained after column chromatography (*n*-pentane–Et_2O, 4:1) as colourless crystals.

Yield: 0.175 g (91%); $[\alpha]_D^{22}$ –9.52 (*c* 1.04, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**4e**.

Hydroxy Ketones 6a,b; General Procedure (GP3)

First, $CeCl_3 \cdot 7H_2O$ (2 equiv) was dried without stirring at 130 °C in vacuo (ca. 0.05 mbar) for 1 h. It was subsequently ground by stirring under these conditions for another 1 h. After cooling to r.t., the flask was filled with argon, and anhyd THF (4 mL/mmol $CeCl_3$) was added. The suspension was stirred for at least 1 h and then placed in an ultrasound bath for another 1 h. The mixture was cooled to –78 °C, and RLi in (n-Bu)$_2$O (R = Ph) or *n*-pentane–THF (R = Naph) (2 equiv) was added dropwise. After the mixture had stirred at low temperature for 2 h, a bright yellow colour indicated the formation of the active cerium reagent. The mixture was then cooled to –105 °C and lactone **4a** was added in anhyd THF (5 mL/mmol), while the temperature was carefully kept below –100 °C. After 30 min, the reaction mixture was allowed to warm to –99 °C and quenched with H_2O (10 mL/mmol). Extraction with CH_2Cl_2 (100 mL/mmol), followed by treatment with brine and drying ($MgSO_4$) provided the desired product **6**, which could be purified by column chromatography.

(3*S*,4*S*)-3,5-Bis(*tert*-butyldimethylsiloxy)-4-hydroxy-4-methyl-1-phenylpentan-1-one [(*S*,*S*)-6a]

According to GP3, lactone (*S*,*S*)-**4a** (0.375 g, 1.00 mmol) was treated with PhLi and $CeCl_3$. Workup and column chromatography (*n*-pentane–Et_2O, 6:1) gave pure product (*S*,*S*)-**6a** as a colourless oil.

Yield: 0.246 g (54%); $[\alpha]_D^{24}$ +5.6 (*c* 0.65, $CHCl_3$); R_f = 0.6 (*n*-pentane–Et_2O, 4:1).

IR (film): 2932, 2859, 1689, 1468, 1367, 1255, 1088, 941, 838, 778, 691, 672 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.08 (s, 6 H, SiCH_3), 0.15 (s, 3 H, SiCH_3), 0.16 (s, 3 H, SiCH_3), 0.92 [s, 9 H, C(CH_3)$_3$], 1.00 [s, 9 H, C(CH_3)$_3$], 1.20 (s, 3 H, CCH_3), 2.69 (s, 1 H, OH), 3.11 (dd, *J* = 17.3, 6.3 Hz, 1 H, CH_2CO), 3.49 (dd, *J* = 17.3, 4.4 Hz, 1 H, CH_2CO), 3.59 (d, *J* = 9.6 Hz, 1 H, CH_2OSi), 3.63 (d, *J* = 9.6 Hz, 1 H, CH_2OSi), 4.67 (dd, *J* = 6.3, 4.4 Hz, 1 H, C*H*CH$_2$CO), 7.52–7.55 (m, 2 H, CCHC*H*), 7.62–7.65 (m, 1 H, CCHCHC*H*), 8.04–8.06 (m, 2 H, CC*H*CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.5, –5.4, –4.9, –4.3, 18.1, 21.1, 25.9, 26.0, 42.0, 67.3, 71.6, 74.4, 128.0, 128.4, 132.8, 137.1, 198.1.

MS (CI): *m*/*z* (%) = 435 (100), 437 (12).

Anal. Calcd for $C_{24}H_{44}O_4Si_2$: C, 63.66; H, 9.80. Found: C, 63.95; H, 10.05.

(3*R*,4*R*)-3,5-Bis(*tert*-butyldimethylsiloxy)-4-hydroxy-4-methyl-1-phenylpentan-1-one [(*R*,*R*)-6a]

According to GP4, lactone (*R*,*R*)-**4a** (0.375 g, 1.00 mmol) was treated with PhLi and $CeCl_3$. Workup and column chromatography (*n*-pentane–Et_2O, 6:1) gave pure product (*R*,*R*)-**6a** as a colourless oil.

Yield: 0.372 g (82%); $[\alpha]_D^{25}$ –13.3 (*c* 1.07, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**6a**.

(3*S*,4*S*)-3,5-Bis(*tert*-butyldimethylsiloxy)-4-hydroxy-4-methyl-1-(1-naphthyl)-pentan-1-one [(*S*,*S*)-6b]

According to GP3, lactone (*S*,*S*)-**4a** (0.0.375 g, 1.00 mmol) was treated with 1-NaphLi [freshly prepared by addition of *t*-BuLi (2 equiv) to a soln of 1-BrNaph in anhyd THF (5 mL/mmol) at –78 °C] and $CeCl_3$. Workup and column chromatography (*n*-pentane–Et_2O, 6:1) gave pure product (*S*,*S*)-**6b** as a colourless oil.

Yield: 0.502 g (100%); $[\alpha]_D^{23}$ –33.2 (*c* 1.57, $CHCl_3$); R_f = 0.5 (*n*-pentane–Et_2O, 6:1).

IR (film): 2951, 2890, 2859, 1683, 1467, 1365, 1255, 1087, 839, 765, 670 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.02 (s, 3 H, SiCH_3), 0.07 (2s, 6 H, SiCH_3), 0.19 (s, 3 H, SiCH_3), 0.88 [s, 9 H, C(CH_3)$_3$], 0.91 [s, 9 H, C(CH_3)$_3$], 1.16 [s, 3 H, C(CH_3)$_3$], 2.62 (s, 1 H, OH), 3.16 (dd, *J* = 17.3, 6.0 Hz, 1 H, CH_2CO), 3.49 (dd, *J* = 17.3, 5.0 Hz, 1 H, CH_2CO), 3.54 (s, 2 H, CH_2OSi), 4.67 (dd, *J* = 6.0, 5.0 Hz, 1 H, C*H*CH$_2$CO), 7.48–8.65 (m, 7 H, *H*Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.5, –5.4, –4.9, –4.1, 18.2, 18.2, 21.3, 25.9, 26.0, 45.6, 67.3, 71.8, 74.4, 124.1, 125.7, 126.2, 127.2, 127.7, 127.8, 128.2, 132.5, 130.0, 133.8, 136.0, 201.7.

MS (CI): *m*/*z* (%) = 353 (100), 488 (6).

HRMS: *m*/*z* [M – OH]$^+$ calcd for $C_{28}H_{45}O_3Si_2$: 485.291; found: 485.291.

Anal. Calcd for $C_{28}H_{46}O_4Si_2$: C, 66.88; H, 9.22. Found: C, 67.29; H, 9.03.

(3*R*,4*R*)-3,5-Bis(*tert*-butyldimethylsiloxy)-4-hydroxy-4-methyl-1-(1-naphthyl)pentan-1-one [(*R*,*R*)-6b]

According to GP3, lactone (*R*,*R*)-**4a** (0.375 g, 1.00 mmol) was treated with 1-NaphLi [freshly prepared by addition of *t*-BuLi (2 equiv) to a soln of 1-BrNaph in anhyd THF (5 mL/mmol) at –78 °C] and $CeCl_3$. Workup and column chromatography (*n*-pentane–Et_2O, 6:1) gave the pure product (*R*,*R*)-**6b** as a colourless oil.

Yield: 0.502 g (100%); $[\alpha]_D^{25}$ +19.5 (*c* 2.09, $CHCl_3$); all other data correspond with those of (*S*,*S*)-**6b**.

TBS-Protected *C*-Nucleosides 7a,b; General Procedure (GP4)

A suspension of $Me_4N^+[HB(OAc)_3]^-$ (3 equiv) in anhyd MeCN (5 mL/mmol) was treated with anhyd AcOH (5 mL/mmol) under an argon atmosphere. The resulting soln was cooled to –30 °C and added to a soln of the appropriate hydroxy ketone **6** in anhyd MeCN (2.5 mL/mmol). The reaction was left overnight at –26 °C. Quenching of the reaction with a soln of Na/K tartrate in H_2O (10 mL/mmol) led to a precipitate, which was dissolved by the addition of sat. aq Na_2CO_3. The aqueous phase was extracted with Et_2O (100 mL/mmol) and the combined organic layers were washed with brine and dried ($MgSO_4$). The cyclised products **7** were purified by column chromatography.

(2*S*,3*S*,5*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-methyl-5-phenyltetrahydrofuran [(*S*,*S*,*S*)-7a]

The hydroxy ketone (*S*,*S*)-**6a** (0.074 g, 0.16 mmol) was treated with $Me_4N^+[HB(OAc)_3]^-$ according to GP4. The pure TBS-protected *C*-nucleoside (*S*,*S*,*S*)-**7a** was obtained as a colourless oil after workup and column chromatography (*n*-pentane–Et_2O, 40:1).

Yield: 0.046 g (69%); $[\alpha]_D^{25}$ +7.2 (*c* 1.40, $CHCl_3$); R_f = 0.5 (*n*-pentane–Et_2O, 40:1).

IR (film): 2932, 2888, 2858, 1466, 1363, 1255, 1098, 1028, 941, 838, 777, 698, 673 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 6 H, $SiCH_3$), 0.07 (s, 6 H, $SiCH_3$), 0.86 [s, 9 H, $C(CH_3)_3$], 0.91 [s, 9 H, $C(CH_3)_3$], 1.21 (s, 3 H, CH_3), 1.99 (ddd, *J* = 12.9, 7.4, 5.4 Hz, 1 H, $CCHCH_2CH$), 2.58 (ddd, *J* = 12.9, 7.7, 5.7 Hz, 1 H, $CCHCH_2CH$), 3.69 (d, *J* = 10.1 Hz, 1 H, CH_2OSi), 3.82 (d, *J* = 10.1 Hz, 1 H, CH_2OSi), 4.16 (dd, *J* = 5.7, 5.7 Hz, 1 H, $CCHCH_2CH$), 5.02 (dd, *J* = 7.7, 7.7 Hz, 1 H, $CCHCH_2CH$), 7.20–7.46 (m, 5 H, *H*Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.4, –5.1, –4.7, 18.0, 18.5, 21.5, 25.7, 26.1, 43.9, 66.2, 77.0, 78.2, 85.3, 126.2, 128.1, 127.0, 143.8.

MS (EI): *m*/*z* (%) = 231 (100), 437 (1) [M + H$^+$].

Anal. Calcd for $C_{24}H_{44}O_3Si_2$: C, 66.00; H, 10.15. Found: C, 65.65; H, 10.15.

(2*R*,3*R*,5*R*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-methyl-5-phenyltetrahydrofuran [(*R*,*R*,*R*)-7a]
The hydroxy lactone (*R*,*R*)-**6a** (0.158 g, 0.35 mmol) was treated with $Me_4N^+[HB(OAc)_3]^-$ according to GP4. The pure TBS-protected *C*-nucleoside (*R*,*R*,*R*)-**7a** was obtained as a colourless oil after workup and column chromatography (*n*-pentane–Et_2O, 40:1).

Yield: 0.108 g (70%); $[\alpha]_D^{25}$ –6.8 (*c* 1.03, $CHCl_3$); all other data correspond with those of (*S*,*S*,*S*)-**7a**.

(2*S*,3*S*,5*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-methyl-5-(1-naphthyl)tetrahydrofuran [(*S*,*S*,*S*)-7b]
The hydroxy lactone (*S*,*S*)-**6b** (0.328 g, 0.67 mmol) was treated with $Me_4N^+[HB(OAc)_3]^-$ according to GP4. The pure TBS-protected *C*-nucleoside (*S*,*S*,*S*)-**7b** was obtained as a colourless oil after workup and column chromatography (*n*-pentane–Et_2O, 40:1).

Yield: 0.215 g (66%); $[\alpha]_D^{25}$ –42.1 (*c* 1.06, $CHCl_3$); all other data correspond with those of (*R*,*R*,*R*)-**7b**.

(2*R*,3*R*,5*R*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-methyl-5-(1-naphthyl)tetrahydrofuran [(*R*,*R*,*R*)-7b]
The hydroxy lactone (*R*,*R*)-**6b** (0.502 g, 1.00 mmol) was treated with $Me_4N^+[HB(OAc)_3]^-$ according to GP4. The pure TBS-protected *C*-nucleoside (*R*,*R*,*R*)-**7b** was obtained as a colourless oil after workup and column chromatography (*n*-pentane–Et_2O, 40:1).

Yield: 0.451 g (93%); $[\alpha]_D^{24}$ +43.9 (*c* 0.95, $CHCl_3$); R_f = 0.5 (*n*-pentane–Et_2O, 40:1).

IR ($CHCl_3$): 2953, 2931, 2886, 2858, 1467, 1255, 1217, 1100, 840, 760 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.12 (s, 3 H, $SiCH_3$), 0.17 (s, 3 H, $SiCH_3$), 0.23 (s, 6 H, $SiCH_3$), 0.91 [s, 9 H, $C(CH_3)_3$], 1.06 [s, 9 H, $C(CH_3)_3$], 1.48 (s, 3 H, CH_3), 2.01 (ddd, *J* = 12.8, 7.2, 5.6 Hz, 1 H, $CCHCH_2CH$), 2.90 (ddd, *J* = 12.8, 7.6, 6.0 Hz, 1 H, $CCHCH_2CH$), 3.83 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 3.94 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.28 (dd, *J* = 6.0, 5.6 Hz, 1 H, $CCHCH_2CH$), 5.81 (dd, *J* = 7.6, 7.2 Hz, 1 H, $CCHCH_2CH$), 7.46–7.99 (m, 7 H, *H*Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.3, –5.3, –5.1, –4.7, 17.9, 18.4, 21.5, 25.6, 26.0, 42.9, 65.9, 74.4, 78.0, 85.0, 122.6, 122.9, 124.8, 125.3, 125.5, 126.9, 128.6, 129.8, 133.3, 139.3.

MS (CI): *m*/*z* (%) = 167 (100), 488 (4) [M + H$^+$].

Anal. Calcd for $C_{28}H_{46}O_3Si_2$: C, 69.08; H, 9.52. Found: C, 69.50; H, 9.71.

Free *C*-Nucleosides 8a,b; General Procedure (GP5)
A TFA–$CHCl_3$ mixture (4:1, 2.5 mL/mmol) was slowly added to the appropriate TBS-protected nucleoside **7** in $CHCl_3$ (6 mL/mmol) at 0 °C. When the reaction was completed, the solvent was evaporated under reduced pressure. Traces of TFA were removed by co-evaporation with MeOH. Column chromatography gave pure products **8**.

(2*S*,3*S*,5*S*)-2-(Hydroxymethyl)-2-methyl-5-phenyltetrahydrofuran-3-ol [(*S*,*S*,*S*)-8a]
As described in GP5, silyl ether (*S*,*S*,*S*)-**7a** (0.046 g, 0.11 mmol) was desilylated in TFA–$CHCl_3$. After column chromatography (Et_2O), the free nucleoside (*S*,*S*,*S*)-**8a** was obtained as a colourless foam.

Yield: 0.008 g (35%); the analytical data correspond with those of (*R*,*R*,*R*)-**8a**.

(2*R*,3*R*,5*R*)-2-(Hydroxymethyl)-2-methyl-5-phenyltetrahydrofuran-3-ol [(*R*,*R*,*R*)-8a]
As described in GP5, the silyl ether (*R*,*R*,*R*)-**7a** (0.111 g, 0.25 mmol) was desilylated in TFA–$CHCl_3$. After column chromatography (Et_2O), the free nucleoside (*R*,*R*,*R*)-**8a** was obtained as a colourless foam.

Yield: 0.034 g (65%); $[\alpha]_D^{23}$ +17.0 (*c* 0.24, $CHCl_3$); R_f = 0.5 (Et_2O).

IR (KBr): 3502, 3363, 2920, 2868, 1496, 1457, 1370, 1209, 1067, 1009, 938, 906, 753, 698, 619 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (s, 3 H, CH_3), 1.97 (ddd, *J* = 12.9, 9.6, 4.9 Hz, 1 H, CH_2CH), 2.67 (s, 1 H, OH), 2.70 (dd, *J* = 12.9, 6.3 Hz, 1 H, CH_2CH), 3.79 (s, 2 H, CH_2OH), 4.28 (dd, *J* = 14.0, 7.1 Hz, 1 H, *CH*OH), 4.94 (dd, *J* = 9.6, 6.3 Hz, 1 H, $CHCH_2CHOH$), 7.26–7.42 (m, 5 H, *H*Ar)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.9, 44.7, 66.9, 76.7, 79.8, 83.5, 126.0, 127.7, 128.3, 141.2.

MS (EI): *m*/*z* (%) = 177 (100), 209 (1) [M + H$^+$].

HRMS: *m*/*z* [M]$^+$ calcd for $C_{12}H_{16}O_3$: 208.110; found: 208.110.

(2*S*,3*S*,5*S*)-2-(Hydroxymethyl)-2-methyl-5-(1-naphthyl)tetrahydrofuran-3-ol [(*S*,*S*,*S*)-8b]
As described in GP5, the silyl ether (*S*,*S*,*S*)-**7b** (0.215 g, 0.44 mmol) was desilylated in TFA–$CHCl_3$. After column chromatography (Et_2O), the free nucleoside (*S*,*S*,*S*)-**8b** was obtained as colourless crystals.

Yield: 0.061 g (54%); $[\alpha]_D^{22}$ –25.0 (*c* 0.96, $CHCl_3$); all other analytical data correspond with those of (*R*,*R*,*R*)-**8b**.

(2*R*,3*R*,5*R*)-2-(Hydroxymethyl)-2-methyl-5-(1-naphthyl)tetrahydrofuran-3-ol [(*R*,*R*,*R*)-8b]
As described in GP5, the silyl ether (*R*,*R*,*R*)-**7b** (0.240 g, 0.49 mmol) was desilylated in TFA–$CHCl_3$. After column chromatography (Et_2O), the free nucleoside (*R*,*R*,*R*)-**8b** was obtained as colourless crystals.

Yield: 0.076 g (60%); mp 118 °C; $[\alpha]_D^{25}$ +26.3 (*c* 0.99, $CHCl_3$); R_f = 0.5 (Et_2O).

IR (KBr): 3517, 3325, 2962, 2913, 2862, 1508, 1435, 1373, 1340, 1283, 1220, 1101, 1055, 1016, 939, 913, 860, 778, 490 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 3 H, CH_3), 2.05 (ddd, *J* = 12.9, 9.3, 6.6 Hz, 1 H, CH_2CH), 2.42 (t, *J* = 6.2 Hz, 1 H, CH_2OH), 2.91 (ddd, *J* = 12.9, 6.6, 6.3 Hz, 1 H, CH_2CH), 2.99 (d, *J* = 14.5 Hz, 1 H, CHO*H*), 3.87 (d, *J* = 6.2 Hz, 2 H, CH_2OH), 4.36 (dd, *J* = 14.5, 6.59 Hz, 1 H, *CH*OH), 5.67 (dd, *J* = 9.3, 6.3 Hz, 1 H, $CHCH_2CHOH$), 7.45–7.99 (m, 7 H, *H*Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0, 43.7, 66.9, 73.3, 79.7, 83.6, 121.7, 123.1, 125.4, 125.9, 127.9, 128.6, 130.5, 133.5, 137.1.

MS (EI): *m*/*z* (%) = 258 (100), 259 (17) [M + H$^+$].

Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.36; H, 7.19.

Acylated Lactols 9a–e; General Procedure (GP6)

The appropriate lactone, one of **4a–e**, was dissolved in anhyd CH_2Cl_2 (10 mL/mmol), and at –78 °C DIBAL-H (1.05 equiv) was added dropwise. After the reaction was completed, it was quenched with a sat. soln of Na/K tartrate in H_2O (20 mL/mmol) and a pH 7 buffer (20 mL/mmol). After extraction of the mixture with CH_2Cl_2, treatment with brine, and drying ($MgSO_4$), the oily residue was dissolved in py, and Ac_2O was added at r.t. Stirring overnight and subsequent evaporation of the solvents led to products **9a–e**, which could be purified by column chromatography.

(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl Acetate [(*S*,*S*,*S*)-9a]

According to GP6, lactone (*S*,*S*)-**4a** (0.331 g, 0.87 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*S*,*S*,*S*)-**9a** was obtained as a colourless oil.

Yield: 0.270 g (74%); $[\alpha]_D^{25}$ +30.15 (*c* 1.28, $CHCl_3$); R_f = 0.5 (*n*-pentane–Et_2O, 10:1).

IR (film): 2954, 2894, 2859, 1746, 1468, 1372, 1253, 1113, 1011, 974, 843, 774 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.05 (2 s, 6 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.89 [s, 18 H, $C(CH_3)_3$], 1.23 (s, 3 H, CCH_3), 2.04 (s, 3 H, CH_3CO), 2.16 (ddd, *J* = 13.2, 6.9, 1.9 Hz, 1 H, CH_2CH), 2.40 (ddd, *J* = 13.2, 6.9, 5.8 Hz, 1 H, CH_2CH), 3.56 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 3.64 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.20 (dd, *J* = 6.9, 6.9 Hz, 1 H, CHOH), 6.29 (dd, *J* = 5.8, 1.9 Hz, 1 H, $CHCH_2CHOH$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.5, –5.4, –5.0, –4.7, 18.0, 18.3, 21.4, 22.7, 25.7, 25.9, 41.5, 65.8, 76.2, 86.7, 97.6, 170.2.

MS (CI): *m*/*z* (%) = 227 (100), 421 (2) $[M + 2]^+$.

Anal. Calcd for $C_{20}H_{42}O_5Si_2$: C, 57.37; H, 10.11. Found: C, 57.31; H, 10.13.

(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl Acetate [(*R*,*R*,*R*)-9a]

According to GP6, lactone (*R*,*R*)-**4a** (3.057 g, 8.16 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*R*,*R*,*R*)-**9a** was obtained as a colourless oil.

Yield: 1.843 g (54%); $[\alpha]_D^{25}$ –21.54 (*c* 1.28, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**9a**.

(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-ethyltetrahydrofuran-2-yl Acetate [(*S*,*S*,*S*)-9b]

According to GP6, lactone (*S*,*S*)-**4b** (0.191 g, 0.49 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*S*,*S*,*S*)-**9b** was obtained as a colourless oil.

Yield: 0.132 g (62%); $[\alpha]_D^{25}$ –34.38 (*c* 1.44, $CHCl_3$); R_f = 0.3 (*n*-pentane–Et_2O, 10:1).

IR (film): 2935, 2892, 2859, 1747, 1468, 1371, 1253, 1114, 988, 958, 884, 843, 775 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.04 (2 s, 6 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.89 [m, 21 H, $C(CH_3)_3$, CH_3CH_2], 1.55 (m, 2 H, CH_3CH_2), 2.03 (s, 3 H, CH_3CO), 2.12 (ddd, *J* = 12.9, 7.7, 1.2 Hz, 1 H, CH_2CH), 2.43 (ddd, *J* = 12.9, 7.7, 5.5 Hz, 1 H, CH_2CH), 3.53 (d, *J* = 10.3 Hz, 1 H, CH_2OSi), 7.37 (d, *J* = 10.3 Hz, 1 H, CH_2OSi), 4.30 (dd, *J* = 7.7, 7.7 Hz, 1 H, CHOSi), 6.27 (dd, *J* = 5.5, 1.2 Hz, 1 H, $CHCH_2CHOSi$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.5, –5.4, –5.0, –4.5, 7.7, 17.9, 18.2, 21.4, 25.7, 25.9, 27.1, 41.3, 64.3, 73.3, 88.6, 97.3, 170.2.

MS (CI): *m*/*z* (%) = 241 (100), 432 (0.1) $[M]^+$.

Anal. Calcd for $C_{21}H_{44}O_5Si_2$: C, 58.29; H, 10.25. Found: C, 58.58; H, 10.39

(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-ethyltetrahydrofuran-2-yl Acetate [(*R*,*R*,*R*)-9b]

According to GP6, lactone (*R*,*R*)-**4b** (0.260 g, 0.67 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*R*,*R*,*R*)-**9b** was obtained as a colourless oil.

Yield: 0.156 g (54%); $[\alpha]_D^{22}$ +35.3 (*c* 1.43, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**9b**.

(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-phenyltetrahydrofuran-2-yl Acetate [(*S*,*S*,*S*)-9c]

According to GP6, lactone (*S*,*S*)-**4c** (0.192 g, 0.44 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*S*,*S*,*S*)-**9c** was obtained as a colourless oil.

Yield: 0.200 g (95%); $[\alpha]_D^{24}$ –19.2 (*c* 1.17, $CHCl_3$); R_f = 0.4 (*n*-pentane–Et_2O, 10:1).

IR (film): 2954, 2932, 2891, 2858, 1748, 1468, 1367, 1253, 1113, 1010, 959, 940, 841, 777, 703 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 6 H, $SiCH_3$), 0.16 (s, 3 H, $SiCH_3$), 0.18 (s, 3 H, $SiCH_3$), 0.92 [s, 18 H, $C(CH_3)_3$], 2.06 (s, 3 H, CH_3CO), 2.16 (ddd, *J* = 12.6, 6.9, 1.7 Hz, 1 H, CH_2CH), 2.62 (ddd, *J* = 12.6, 8.2, 5.4 Hz, 1 H, CH_2CH), 3.71 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 4.07 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 4.65 (dd, *J* = 8.2, 6.9 Hz, 1 H, CHOSi), 6.53 (dd, *J* = 5.4, 1.7 Hz, 1 H, $CHCH_2CHOSi$), 7.32–7.52 (m, 5 H, *H*Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.6, –5.0, –4.3, 17.9, 18.2, 21.3, 25.7, 25.9, 41.0, 66.7, 77.2, 89.4, 97.5, 124.8, 126.9, 127.6, 143.2, 170.2.

MS (CI): *m*/*z* (%) = 289 (100), 479 (1) $[M - H^+]$.

Anal. Calcd for $C_{25}H_{44}O_5Si_2$: C, 62.45; H, 9.22. Found: C, 62.80; H, 8.91.

(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-phenyltetrahydrofuran-2-yl Acetate [(*R*,*R*,*R*)-9c]

According to GP6, lactone (*R*,*R*)-**4c** (0.380 g, 0.87 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*R*,*R*,*R*)-**9c** was obtained as a colourless oil.

Yield: 0.261 g (62%); $[\alpha]_D^{24}$ +27.5 (*c* 1.44, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**9c**.

(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-(4-fluorophenyl)tetrahydrofuran-2-yl Acetate [(*S*,*S*,*S*)-9d]

According to GP6, lactone (*S*,*S*)-**4d** (0.049 g, 0.11 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*S*,*S*,*S*)-**9d** was obtained as a colourless oil.

Yield: 0.035 g (64%); $[\alpha]_D^{22}$ –22.9 (*c* 0.72, $CHCl_3$); R_f = 0.3 (*n*-pentane–Et_2O, 10:1).

IR ($CHCl_3$): 2952, 2893, 2860, 1749, 1604, 1510, 1468, 1369, 1251, 1113, 1011, 942, 844, 778, 670, 558 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 6 H, SiCH_3), 0.16 (s, 3 H, SiCH_3), 0.18 (s, 3 H, SiCH_3), 0.91 [s, 9 H, C(CH_3)$_3$], 1.03 [s, 9 H, C(CH_3)$_3$], 2.07 (s, 3 H, CH_3CO), 2.16 (ddd, *J* = 12.6, 6.9, 1.7 Hz, 1 H, CH_2CH), 2.59 (ddd, *J* = 12.6, 8.0, 5.2 Hz, 1 H, CH_2CH), 3.71 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 4.00 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 4.60 (dd, *J* = 8.0, 6.9 Hz, 1 H, C*H*OSi), 6.52 (dd, *J* = 5.2, 1.7 Hz, 1 H, C*H*CH$_2$CHOSi), 7.04–7.09 (m, 2 H, FCCHC*H*), 7.45–7.49 (m, 2 H, FCC*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.6, –5.0, –4.3, 17.9, 18.2, 21.3, 25.7, 25.9, 41.0, 66.6, 76.8, 89.2, 97.5, 114.4 (d, J_{C-F} = 20.6 Hz, 2 C, FC*C*H), 126.6 (d, J_{C-F} = 7.6 Hz, 2 C, FCCH*C*H), 139.0 (d, J_{C-F} = 3.0, 1 C, FCCHCH*C*), 161.78 (d, J_{C-F} = 244.1, 1 C, F*C*), 170.1.

MS (CI): *m*/*z* (%) = 307 (100), 497 (1) [M – H$^+$].

Anal. Calcd for $C_{25}H_{43}FO_5Si_2$: C, 60.20; H, 8.69. Found: C, 60.35; H, 8.88.

(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-(4-fluorophenyl)tetrahydrofuran-2-yl Acetate [(*R*,*R*,*R*)-9d]

According to GP6, lactone (*R*,*R*)-**4d** (0.222 g, 0.49 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*R*,*R*,*R*)-**9d** was obtained as a colourless oil.

Yield: 0.180 g (74%); $[\alpha]_D^{22}$ +28.8 (*c* 0.94, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**9d**.

(2*S*,4*S*,5*S*)-5-Allyl-4-(*tert*-butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]tetrahydrofuran-2-yl Acetate [(*S*,*S*,*S*)-9e]

According to GP6, lactone (*S*,*S*)-**4e** (0.205 g, 0.51 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*S*,*S*,*S*)-**9e** was obtained as a colourless oil.

Yield: 0.167 g (74%); $[\alpha]_D^{22}$ –33.5 (*c* 2.32, $CHCl_3$); R_f = 0.4 (*n*-pentane–Et_2O, 10:1).

IR (film): 2954, 2932, 2892, 2858, 1751, 1469, 1371, 1254, 1115, 1002, 963, 841, 778 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 6 H, SiCH_3), 0.62 (s, 3 H, SiCH_3), 0.72 (s, 3 H, SiCH_3), 0.89 [s, 9 H, C(CH_3)$_3$], 0.90 [s, 9 H, C(CH_3)$_3$], 2.04 (s, 3 H, CH_3CO), 2.12 (ddd, *J* = 12.9, 7.2, 1.2 Hz, 1 H, CH_2CHOSi), 2.29 (m, 2 H, CCH_2CHCH$_2$), 2.42 (ddd, *J* = 12.9, 8.2, 5.7 Hz, 1 H, CH_2CHOSi), 3.52 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 3.69 (d, *J* = 10.6 Hz, 1 H, CH_2OSi), 4.33 (dd, *J* = 8.2, 7.2 Hz, 1 H, C*H*OSi), 5.10 (m, 2 H, CCH$_2$CHCH_2), 5.81 (m, 1 H, CCH$_2$C*H*CH$_2$), 6.28 (dd, *J* = 5.7, 1.2 Hz, 1 H, C*H*CH$_2$CHOSi).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.5, –5.0, –4.5, 17.9, 18.3, 21.4, 25.7, 26.0, 39.3, 41.2, 65.0, 73.4, 87.9, 97.4, 117.9, 133.6, 170.30.

MS (CI): *m*/*z* (%) = 253 (100), 445 (1) [M + H$^+$].

Anal. Calcd for $C_{22}H_{44}O_5Si_2$: C, 59.41; H, 9.97. Found: C, 59.47; H, 9.94.

(2*R*,4*R*,5*R*)-5-Allyl-4-(*tert*-butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]tetrahydrofuran-2-yl Acetate [(*R*,*R*,*R*)-9e]

According to GP6, lactone (*R*,*R*)-**4e** (0.146 g, 0.36 mmol) was reduced and acylated. After workup and column chromatography (*n*-pentane–Et_2O, 10:1), pure product (*R*,*R*,*R*)-**9e** was obtained as a colourless oil.

Yield: 0.102 g (64%); $[\alpha]_D^{22}$ +40.1 (*c* 0.89, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**9e**.

Phenyl Sulfides 10a–e; General Procedure (GP7)

BF_3·OEt_2 (5.0 equiv) and TMSSPh (10.0 equiv) were slowly added to a soln of the appropriate acylated lactol, one of **9a–e**, in *n*-hexane at –95 °C. The mixture was warmed to r.t. overnight and subsequently quenched with sat. aq $NaHCO_3$ (10 mL/mmol). Extraction with Et_2O (50 mL/mmol), treatment with brine, and drying ($MgSO_4$) gave products **10a–e** as anomeric mixtures, which were purified by column chromatography.

(2*S*,3*S*,5*R*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-methyl-5-(phenylsulfanyl)tetrahydrofuran [(*S*,*S*,*R*)-10a]

The nucleophilic substitution was carried out with lactol (*S*,*S*,*S*)-**9a** (0.468 g, 1.12 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*S*,*S*,*R*)-**10a** was characterised.

Yield: 0.452 g (86%); R_f = 0.4 (*n*-pentane–Et_2O, 20:1).

IR (film): 3639, 2936, 2860, 1470, 1255, 1099, 1010, 938, 839, 777, 744 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.07 (s, 6 H, SiCH_3), 0.89 (s, 3 H, SiCH_3), 0.10 (s, 3 H, SiCH_3), 0.92 [s, 9 H, C(CH_3)$_3$], 0.94 [s, 9 H, C(CH_3)$_3$], 1.19 (s, 3 H, CH_3C), 2.15 (ddd, *J* = 13.4, 4.6, 4.3 Hz, 1 H, CH_2CH), 2.69 (ddd, *J* = 13.4, 7.6, 6.1 Hz, 1 H, CH_2CH), 3.78 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 3.85 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.07 (dd, *J* = 6.1, 4.3 Hz, 1 H, C*H*OSi), 5.57 (dd, *J* = 7.6, 4.6 Hz, 1 H, C*H*CH$_2$CHOSi), 7.19 (m, 1 H, *H*Ar), 7.25–7.53 (m, 4 H, *H*Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.3, –5.1, –4.6, 15.3, 18.5, 22.5, 25.8, 29.1, 42.3, 66.0, 77.0, 86.1, 87.6, 126.4, 128.7, 130.7, 135.0.

MS (CI): *m*/*z* (%) = 227 (100), 469 (0.2) [M]$^+$.

Anal. Calcd for $C_{24}H_{44}O_3SSi_2$: C, 61.48; H, 9.46. Found: C, 61.74; H, 9.69.

(2*R*,3*R*,5*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-methyl-5-(phenylsulfanyl)tetrahydrofuran [(*R*,*R*,*S*)-10a]

The nucleophilic substitution was carried out with lactol (*R*,*R*,*R*)-**9a** (0.848 g, 2.03 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*R*,*R*,*S*)-**10a** was characterised; all analytical data correspond with those of (S,*S*,*R*)-**10a**.

Yield: 0.933 g (98%).

(2*S*,3*S*,5*R*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-ethyl-5-(phenylsulfanyl)tetrahydrofuran [(*S*,*S*,*R*)-10b]

The nucleophilic substitution was carried out with lactol (*S*,*S*,*S*)-**9b** (0.132 g, 0.31 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*S*,*S*,*R*)-**10b** was characterised.

Yield: 0.148 g (99%); R_f = 0.5 (*n*-pentane–Et_2O, 20:1).

IR (film): 3420, 2932, 2858, 1583, 1469, 1385, 1255, 1097, 1040, 917, 842, 777, 741, 690, 485 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.06 (s, 6 H, SiCH_3), 0.08 (s, 3 H, SiCH_3), 0.09 (s, 3 H, SiCH_3), 0.91 [s, 9 H, C(CH_3)$_3$], 0.89 (t, *J* = 7.2 Hz, 3 H, CH_3CH$_2$), 0.93 [s, 9 H, C(CH_3)$_3$], 1.56 (m, 2 H, CH$_3$CH_2), 2.13 (ddd, *J* = 13.5, 4.5, 4.0 Hz, 1 H, CH_2CHOSi), 2.62 (ddd, *J* = 13.5, 7.4, 6.0 Hz, 1 H, CH_2CHOSi), 3.75 (d, *J* = 10.7 Hz, 1 H, CH_2OSi), 3.92 (d, *J* = 10.7 Hz, 1 H, CH_2OSi), 4.16 (dd, *J* = 6.1, 4.0 Hz, 1 H, C*H*OSi), 5.54 (dd, *J* = 7.4, 4.5 Hz, 1 H, C*H*CH$_2$CHOSi), 7.18–7.54 (m, 5 H, *H*Ar)

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.3, –5.1, –4.5, 8.3, 18.0, 18.4, 25.7, 26.0, 27.3, 42.7, 64.0, 74.7, 86.0, 89.9, 126.1, 128.4, 130.4, 137.3.

MS (CI): *m*/*z* (%) = 241 (100), 482 (0.1) $[M]^+$.

HRMS: *m*/*z* $[M - C_4H_9]^+$ calcd for $C_{21}H_{37}O_3SSi_2$: 425.200; found: 425.200.

(2*R*,3*R*,5*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-ethyl-5-(phenylsulfanyl)tetrahydrofuran [(*R*,*R*,*S*)-10b]

The nucleophilic substitution was carried out with lactol (*R*,*R*,*R*)-**9b** (0.156 g, 0.36 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*R*,*R*,*S*)-**10b** was characterised; all analytical data correspond with those of (S,*S*,*R*)-**10b**.

Yield: 0.169 g (97%).

(2*S*,3*S*,5*R*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-phenyl-5-(phenylsulfanyl)tetrahydrofuran [(*S*,*S*,*R*)-10c]

The nucleophilic substitution was carried out with lactol (*S*,*S*,*S*)-**9c** (0.030 g, 0.06 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*S*,*S*,*R*)-**10c** was characterised.

Yield: 0.033 g (99%); R_f = 0.7 (*n*-pentane–Et_2O, 20:1).

IR (film): 2953, 2888, 2857, 1582, 1474, 1254, 1191, 1136, 1109, 940, 840, 778, 740, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, SiCH_3), 0.04 (s, 3 H, SiCH_3), 0.27 (s, 3 H, SiCH_3), 0.29 (s, 3 H, SiCH_3), 0.98 [s, 9 H, C(CH_3)$_3$], 1.11 [s, 9 H, C(CH_3)$_3$], 2.25 (ddd, *J* = 12.9, 6.7, 5.2 Hz, 1 H, CH_2CHOSi), 2.67 (ddd, *J* = 12.9, 6.7, 5.2 Hz, 1 H, CH_2CHOSi), 3.99 (d, *J* = 10.1 Hz, 1 H, CH_2OSi), 4.03 (d, *J* = 10.1 Hz, 1 H, CH_2OSi), 4.66 (dd, *J* = 5.2, 5.2 Hz, 1 H, C*H*OSi), 6.04 (dd, *J* = 6.7,6.7 Hz 1 H, C*H*S), 7.37–7.77 (m, 10 H, *H*Ar)

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.8, –5.6, –5.0, –4.5, 18.0, 18.3, 25.8, 25.9, 41.6, 66.5, 76.9, 85.6, 90.8, 125.9, 126.4, 126.8, 127.4, 128.6, 130.5, 137.5, 142.6.

MS (CI): *m*/*z* (%) = 289 (100), 531 (1) $[M]^+$.

Anal. Calcd for $C_{29}H_{46}O_3SSi_2$: C, 65.61; H, 8.73. Found: C, 65.96; H, 8.59.

(2*R*,3*R*,5*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-phenyl-5-(phenylsulfanyl)tetrahydrofuran [(*R*,*R*,*S*)-10c]

The nucleophilic substitution was carried out with lactol (*R*,*R*,*R*)-**9c** (0.247 g, 0.51 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*R*,*R*,*S*)-**10c** was characterised; all analytical data correspond with those of (S,*S*,*R*)-**10c**.

Yield: 0.241 g (89%).

(2*S*,3*S*,5*R*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-(4 fluorophenyl)-5-(phenylsulfanyl)tetrahydrofuran [(*S*,*S*,*R*)-10d]

The nucleophilic substitution was carried out with lactol (*S*,*S*,*S*)-**9d** (0.035 g, 0.07 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*S*,*S*,*R*)-**10d** was characterised.

Yield: 0.025 g (65%); R_f = 0.7 (*n*-pentane–Et_2O, 20:1).

IR (film): 2953, 2932, 2889, 2857, 1508, 1471, 1255, 1229, 1097, 1043, 940, 838, 778, 743 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.02 (s, 3 H, SiCH_3), 0.05 (s, 3 H, SiCH_3), 0.28 (s, 3 H, SiCH_3), 0.29 (s, 3 H, SiCH_3), 0.98 [s, 9 H, C(CH_3)$_3$], 1.11 [s, 9 H, C(CH_3)$_3$], 2.22 (ddd, *J* = 12.9, 6.9, 5.2 Hz, 1 H, CH_2CHOSi), 2.65 (ddd, *J* = 12.9, 6.9, 4.7 Hz, 1 H, CH_2CHOSi), 3.94 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.29 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.63 (dd, *J* = 6.9, 5.2 Hz, 1 H, C*H*OSi), 6.03 (dd, *J* = 6.9, 6.9 Hz, 1 H, C*H*S), 7.14–7.77 (m, 9 H, *H*Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.8, –5.6, –5.0, –4.5, 18.0, 18.3, 25.7, 25.9, 41.5, 66.3, 76.8, 85.6, 90.6, 114.1 (d, J_{C-F} = 20.6 Hz, 2 C, FC*C*H), 126.5, 127.3 (d, J_{C-F} = 8.4 Hz, 2 C, FCCH*C*H), 128.7, 130.4, 135.8, 138.4 (d, J_{C-F} = 3.1 Hz, 1 C, FCCHCH*C*), 162.8 (d, J_{C-F} = 244.9 Hz, 1 C, F*C*).

MS (CI): *m*/*z* (%) = 307 (100), 549 (1) $[M]^+$.

Anal. Calcd for $C_{29}H_{45}FO_3SSi_2$: C, 63.46; H, 8.26. Found: C, 63.47; H, 8.15.

(2*R*,3*R*,5*S*)-3-(*tert*-Butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-2-(4-fluorophenyl)-5-(phenylsulfanyl)tetrahydrofuran [(*R*,*R*,*S*)-10d]

The nucleophilic substitution was carried out with lactol (*R*,*R*,*R*)-**9d** (0.180 g, 0.36 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*R*,*R*,*S*)-**10d** was characterised; all analytical data correspond with those of (S,*S*,*R*)-**10d**.

Yield: 0.197 g (99%).

(2*S*,3*S*,5*R*)-2-Allyl-3-(*tert*-butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-5-(phenylsulfanyl)tetrahydrofuran [(*S*,*S*,*R*)-10e]

The nucleophilic substitution was carried out with lactol (*S*,*S*,*S*)-**9e** (0.167 g, 0.38 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*S*,*S*,*R*)-**10e** was characterised.

Yield: 0.127 g (68%); R_f = 0.5 (*n*-pentane–Et_2O, 20:1).

IR (film): 2933, 2858, 1469, 1440, 1386, 1255, 1100, 1009, 920, 841, 777, 743, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.06 (s, 9 H, SiCH_3), 0.08 (s, 3 H, SiCH_3), 0.92 [s, 9 H, C(CH_3)$_3$], 0.93 [s, 9 H, C(CH_3)$_3$], 2.11 (ddd, *J* = 13.5, 4.5, 4.5 Hz, 1 H, CH_2CHOSi), 2.32 (m, 2 H, CCH_2CHCH$_2$), 2.60 (ddd, *J* = 13.5, 7.1, 6.3 Hz, 1 H, CH_2CHOSi), 3.70 (d, *J* = 10.7 Hz, 1 H, CH_2OSi), 3.97 (d, *J* = 10.7 Hz, 1 H, CH_2OSi), 4.20 (dd, *J* = 6.3, 4.5 Hz, 1 H, C*H*OSi), 5.54 (dd, *J* = 7.1, 4.5 Hz, 1 H, C*H*S), 5.09 (m, 2 H, CCH$_2$CHCH_2), 5.85 (m, 1 H, CCH$_2$C*H*CH$_2$), 7.23–7.55 (m, 5 H, *H*Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.4, –5.3, –5.1, –4.5, 17.9, 18.4, 25.7, 26.0, 39.3, 41.4, 65.1, 74.3, 86.2, 89.1, 117.8, 126.2, 128.4, 130.5, 134.1, 137.1.

MS (CI): *m*/*z* (%) = 385 (100), 495 (4) $[M + H^+]$.

HRMS: *m*/*z* $[M - C_4H_9]^+$ calcd for $C_{22}H_{37}O_3SSi_2$: 437.200; found: 437.201.

(2*R*,3*R*,5*S*)-2-Allyl-3-(*tert*-butyldimethylsiloxy)-2-[(*tert*-butyldimethylsiloxy)methyl]-5-(phenylsulfanyl)tetrahydrofuran [(*R*,*R*,*S*)-10e]

The nucleophilic substitution was carried out with lactol (*R*,*R*,*R*)-**9e** (0.102 g, 0.23 mmol) as described in GP7. Column chromatography (*n*-pentane–Et_2O, 40:1) gave a colourless oil as an anomeric mixture, of which the major diastereomer (*R*,*R*,*S*)-**10e** was characterised; all analytical data correspond with those of (S,*S*,*R*)-**10e**.

Yield: 0.087 g (76%).

TBS-Protected *N*-Nucleosides 11–15; General Procedure (GP8)
A suspension of phenyl sulfide **10**, the appropriate silylated nucleobase (2 equiv) and 4-Å MS (125 mg/mmol) in CH_2Cl_2 (10 mL/mmol) was prepared and cooled to –78 °C. Then, NBS (1.2 equiv) was added, and after 1 h, the reaction mixture was warmed to –26 °C and left at this temperature overnight. The reaction was then quenched by the addition of 10% aq $Na_2S_2O_3$ (10 mL/mmol) and filtered. The aqueous phase was extracted with CH_2CL_2 (50 mL/mmol), washed with brine, and dried ($MgSO_4$). Column chromatography gave the TBS-protected *N*-nucleosides **11**–**15**.

1-{(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*S*,*S*,*S*)-11a]
Phenyl sulfide (*S*,*S*,*R*)-**10a** (0.183 g, 0.39 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*S*,*S*,*S*)-**11a** was obtained as colourless crystals.

Yield: 0.146 g (77%); mp 153 °C; $[\alpha]_D^{26}$ +7.5 (*c* 1.02, $CHCl_3$); R_f = 0.9 (*n*-pentane–Et_2O, 1:1).

IR (KBr): 2934, 2858, 1713, 1471, 1285, 1258, 1091, 1011, 930, 842, 777 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 6 H, SiCH_3), 0.06 (s, 3 H, SiCH_3), 0.10 (s, 3 H, SiCH_3), 0.89 [s, 9 H, C(CH_3)$_3$], 0.93 [s, 9 H, C(CH_3)$_3$], 1.21 (s, 3 H, CH_3C), 1.93 (d, *J* = 1.1 Hz, 3 H, CH_3CO), 1.99 (ddd, *J* = 14.6, 2.7, 1.9 Hz, 1 H, CH_2CHOSi), 2.82 (ddd, *J* = 14.6, 7.7, 5.2 Hz, 1 H, CH_2CHOSi), 3.75 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 3.89 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.09 (dd, *J* = 5.2, 1.9 Hz, 1 H, C*H*OSi), 6.21 (dd, *J* = 7.7, 2.7 Hz, 1 H, CH_2C*H*NCO), 7.66 (d, *J* = 1.1 Hz, 1 H, NC*H*CCO), 9.05 (s, 1 H, N*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.4, –5.2, –5.1, –4.9, 12.6, 18.0, 18.4, 21.3, 25.6, 26.0, 41.7, 65.0, 75.1, 83.8, 88.5, 109.8, 136.5, 150.3, 163.7.

MS (EI): *m*/*z* (%) = 73 (100), 485 (2) [M + H^+].

Anal. Calcd for $C_{23}H_{44}O_5N_2Si_2$: C, 56.98; H, 9.15; N, 5.78. Found: C, 56.48; H, 8.74; N, 5.46.

1-{(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*R*,*R*,*R*)-11a]
Phenyl sulfide (*R*,*R*,*S*)-**10a** (0.100 g, 0.21 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*R*,*R*,*R*)-**11a** was obtained as colourless crystals.

Yield: 0.078 g (77%); $[\alpha]_D^{22}$ –6.0 (*c* 1.02, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**11a**.

1-{(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-ethyltetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*S*,*S*,*S*)-11b]
Phenyl sulfide (*S*,*S*,*R*)-**10b** (0.148 g, 0.31 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*S*,*S*,*S*)-**11b** was obtained as colourless crystals.

Yield: 0.136 g (88%); mp 137 °C; $[\alpha]_D^{21}$ +10.4 (*c* 1.20, $CHCl_3$); R_f = 0.3 (*n*-pentane–Et_2O, 1:1).

IR (KBr): 2954, 2859, 2362, 1704, 1470, 1417, 1275, 1194, 1086, 1031, 1006, 838, 775, 736 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.06 (s, 3 H, SiCH_3), 0.09 (s, 3 H, SiCH_3), 0.10 (s, 6 H, SiCH_3), 0.88 [s, 9 H, C(CH_3)$_3$], 0.92 [s, 9 H, C(CH_3)$_3$], 0.93 (m, 3 H, CH_3CH$_2$), 1.57 (m, 2 H, CH$_3$CH_2), 1.92 (d, *J* = 1.1 Hz, 3 H, CH_3CO), 1.96 (ddd, *J* = 14.6, 3.6, 2.2 Hz, 1 H, CH_2CHOSi), 3.75 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 3.86 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 2.77 (dd, *J* = 5.5, 2.2 Hz, 1 H, C*H*OSi), 6.13 (dd, *J* = 7.7, 3.6 Hz, 1 H, CH_2C*H*NCO), 7.67 (d, *J* = 1.1 Hz, 1 H, NC*H*CCO), 8.10 (s, 1 H, N*H*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.5, –5.2, –5.1, –4.8, 8.0, 12.6, 18.0, 18.3, 25.7, 15.9, 26.0, 42.0, 61.9, 73.8, 83.8, 90.9, 110.0, 136.0, 150.2, 163.6.

MS (CI): *m*/*z* (%) = 241 (100), 500 (17) [M + H^+].

HRMS *m*/*z*: [M – C_4H_9]$^+$ calcd for $C_{20}H_{37}O_5N_2Si_2$: 441.224; found: 441.224.

1-{(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-ethyltetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*R*,*R*,*R*)-11b]
Phenyl sulfide (*R*,*R*,*S*)-**10b** (0.169 g, 0.35 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*R*,*R*,*R*)-**11b** was obtained as colourless crystals.

Yield: 0.165 g (95%); $[\alpha]_D^{21}$ –11.3 (*c* 1.07, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**11b**.

1-{(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-phenyltetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*S*,*S*,*S*)-11c]
Phenyl sulfide (*S*,*S*,*R*)-**10c** (0.033 g, 0.06 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*S*,*S*,*S*)-**11c** was obtained as colourless crystals.

Yield: 0.024 g (73%); mp 235 °C; $[\alpha]_D^{23}$ +34.2 (*c* 0.77, $CHCl_3$); R_f = 0.2 (*n*-pentane–Et_2O, 1:1).

IR (KBr): 3027, 2954, 2858, 1668, 1471, 1272, 1189, 1103, 1065, 1006, 936, 837, 779, 704 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.22 (s, 6 H, SiCH_3), 0.38 (s, 3 H, SiCH_3), 0.44 (s, 3 H, SiCH_3), 0.98 [s, 9 H, C(CH_3)$_3$], 1.16 [s, 9 H, C(CH_3)$_3$], 2.08 (2 m, *J* = 14.6 Hz, 1 H, CH_2CHOSi), 2.18 (d, *J* = 1.1 Hz, 3 H, CH_3CO), 2.58 (ddd, *J* = 14.6, 8.2, 5.0 Hz, 1 H, CH_2CHOSi), 4.03 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.43 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.87 (m, 1 H, C*H*OSi), 6.48 (dd, *J* = 8.2, 2.5 Hz, 1 H, CH_2C*H*NCO), 7.48–7.64 (m, 5 H, *H*Ar), 8.06 (d, *J* = 1.1 Hz, 1 H, NC*H*CCO), 9.58 (s, 1 H, N*H*).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –6.0, –5.7, –5.0, –4.9, 12.7, 18.1, 18.4, 25.7, 25.9, 41.1, 65.7, 75.4, 83.4, 91.9, 110.9, 125.7, 128.0, 127.5, 136.8, 140.0, 150.5, 163.9.

MS (CI): *m*/*z* (%) = 547 (100) [M^+], 548 (40) [M + H^+].

Anal. Calcd for $C_{28}H_{46}O_5N_2Si_2$: C, 61.50; H, 8.48; N, 5.12. Found: C, 61.39; H, 8.63; N, 5.11.

1-{(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-phenyltetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*R*,*R*,*R*)-11c]
Phenyl sulfide (*R*,*R*,*S*)-**10c** (0.241 g, 0.45 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*R*,*R*,*R*)-**11c** was obtained as colourless crystals.

Yield: 0.214 g (87%); $[\alpha]_D^{23}$ –37.1 (*c* 1.05, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**11c**.

1-{(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-(4-fluorophenyl)tetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*S*,*S*,*S*)-11d]
Phenyl sulfide (*S*,*S*,*R*)-**10d** (0.025 g, 0.05 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*S*,*S*,*S*)-**11d** was obtained as colourless crystals.

Yield: 0.015 g (53%); mp 233 °C; $[\alpha]_D^{21}$ +33.1 (*c* 0.77, $CHCl_3$); R_f = 0.3 (*n*-pentane–Et_2O, 1:1).

IR (KBr): 3415, 2953, 2857, 2361, 2337, 1712, 1664, 1507, 1473, 1271, 1105, 1066, 1003, 935, 838, 778, 665, 551 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 6 H, SiCH_3), 0.16 (s, 3 H, SiCH_3), 0.22 (s, 3 H, SiCH_3), 0.77 [s, 9 H, C(CH_3)$_3$], 0.94 [s, 9 H, C(CH_3)$_3$], 1.87 (2 m, *J* = 14.6 Hz, 1 H, CH_2CHOSi), 1.96 (d, *J* = 1.2 Hz, 3 H, CH_3CO), 2.35 (ddd, *J* = 14.6, 8.2, 4.9 Hz, 1 H, CH_2CHOSi), 3.76 (d, *J* = 9.9 Hz, 1 H, CH_2OSi), 4.17 (d, *J* = 9.9 Hz, 1 H, CH_2OSi), 4.61 (m, 1 H, C*H*OSi), 6.23 (dd, *J* = 8.1, 2.5 Hz, 1 H, CH$_2$C*H*NCO), 7.05–7.38 (2 m, 4 H, *H*Ar), 7.81 (d, *J* = 1.2 Hz, 1 H, NC*H*CCO), 8.16 (s, 1 H, N*H*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –6.0, –5.7, –5.0, –4.9, 12.7, 18.2, 18.4, 25.7, 25.9, 41.1, 65.6, 75.4, 83.4, 91.7, 110.4, 115.2 (d, J_{C-F} = 21.2 Hz, 2 C, FC*C*H), 127.7 (d, J_{C-F} = 8.0 Hz, 2 C, FC-CH*C*H), 136.0 (d, J_{C-F} = 2.8 Hz, 1 C, FCCHCH*C*), 136.8, 150.7, 162.4 (d, J_{C-F} = 246.8 Hz, 1 C, F*C*), 164.1.

MS (CI): *m*/*z* (%) = 565 (100), 566 (36) [M + H^+].

Anal. Calcd for $C_{28}H_{45}FO_5N_2Si_2$: C, 59.54; H, 8.03; N, 4.96. Found: C, 59.79; H, 7.96; N, 5.01.

1-{(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-(4-fluorophenyl)tetrahydrofuran-2-yl}-5-methylpyrimidine-2,4(1*H*,3*H*)-dione [(*R*,*R*,*R*)-11d]

Phenyl sulfide (*R*,*R*,*S*)-**10d** (0.179 g, 0.33 mmol) was treated with bis-TMS-thymine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*R*,*R*,*R*)-**11d** was obtained as colourless crystals.

Yield: 0.137 g (76%); $[\alpha]_D^{21}$ –33.7 (*c* 1.11, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**11d**.

4-Amino-1-{(2*S*,4*S*,5*S*)-4-(*tert*-butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}pyrimidin-2(1*H*)-one [(*S*,*S*,*S*)-12]

Phenyl sulfide (*S*,*S*,*R*)-**10a** (0.198 g, 0.42 mmol) was treated with bis-TMS-cytosine according to GP8. After column chromatography (EtOAc-MeOH, 20:1), product (*S*,*S*,*S*)-**12** was obtained as colourless crystals.

Yield: 0.099 g (50%); mp >210 °C; $[\alpha]_D^{26}$ –26.9 (*c* 1.04, $CHCl_3$); R_f = 0.3 (EtOAc–MeOH, 20:1).

IR (KBr): 3930, 3894, 3504, 3478, 3371, 2955, 2932, 2890, 2859, 1662, 1626, 1521, 1487, 1410, 1361, 1288, 1256, 1098, 917, 837, 781 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, SiCH_3), 0.07 (s, 3 H, SiCH_3), 0.09 (s, 6 H, SiCH_3), 0.85 [s, 9 H, C(CH_3)$_3$], 0.92 [s, 9 H, C(CH_3)$_3$], 1.22 (s, 3 H, CH_3C), 2.00 (ddd, *J* = 14.3, 3.1, 3.1 Hz, 1 H, CH_2CHOSi), 2.84 (ddd, *J* = 14.3, 7.3, 5.3 Hz, 1 H, CH_2CHOSi), 3.70 (d, *J* = 10.3 Hz, 1 H, CH_2OSi), 3.87 (d, *J* = 10.3 Hz, 1 H, CH_2OSi), 4.09 (dd, *J* = 5.3, 3.1 Hz, 1 H, C*H*OSi), 5.71 (d, *J* = 7.4 Hz, 1 H, C*H*CNH$_2$), 6.15 (dd, *J* = 7.3, 3.1 Hz, 1 H, CH$_2$C*H*NCO), 7.90 (d, *J* = 7.4 Hz, 1 H, C*H*CHCNH$_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.4, –5.3, –5.2, –4.7, 18.0, 18.4, 21.7, 25.7, 26.0, 41.9, 65.2, 75.6, 85.2, 88.3, 93.4, 142.1, 155.9, 165.6.

MS (CI): *m*/*z* (%) = 227 (100), 471 (25) [M + H^+].

HRMS: *m*/*z* [M –C_4H_9]$^+$ calcd for $C_{18}H_{34}N_3O_4Si_2$: 412.209; found: 412.209.

4-Amino-1-{(2*R*,4*R*,5*R*)-4-(*tert*-butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}pyrimidin-2(1*H*)-one [(*R*,*R*,*R*)-12]

Phenyl sulfide (*R*,*R*,*S*)-**10a** (0.199 g, 0.42 mmol) was treated with bis-TMS-cytosine according to GP8. After column chromatography (EtOAc-MeOH, 20:1), product (*R*,*R*,*R*)-**12** was obtained as colourless crystals.

Yield: 0.095 g (48%); $[\alpha]_D^{23}$ +29.1 (*c* 1.02, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**12**.

***N*-(9-{(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-6-oxo-6,9-dihydro-1*H*-purin-2-yl)acetamide [(*S*,*S*,*S*)-13]**

Phenyl sulfide (*S*,*S*,*R*)-**10a** (0.096 g, 0.20 mmol) was treated with tris-TMS-*N*-Ac-guanine according to GP8. After column chromatography (EtOAc), product (*S*,*S*,*S*)-**13** was obtained as colourless crystals.

Yield: 0.051 g (46%); mp 162 °C; R_f = 0.6 (EtOAc).

IR (KBr): 3167, 2934, 2858, 1697, 1617, 1466, 1373, 1256, 1192, 1098, 840, 779, 641 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 3 H, SiCH_3), 0.09 (s, 3 H, SiCH_3), 0.14 (s, 3 H, SiCH_3), 0.18 (s, 3 H, SiCH_3), 0.86 [s, 9 H, C(CH_3)$_3$], 1.00 [s, 9 H, C(CH_3)$_3$], 1.36 (s, 3 H, CCH_3), 2.49 (s, 3 H, CH_3CONH), 2.35 (ddd, *J* = 14.3, 2.2, 2.2 Hz, 1 H, CH_2CHOSi), 3.06 (ddd, *J* = 14.3 Hz, ^3J = 6.9, 5.2 Hz, 1 H, CH_2CHOSi), 3.88 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 4.02 (d, *J* = 10.4 Hz, 1 H, CH_2OSi), 4.25 (dd, *J* = 5.2, 2.2 Hz, 1 H, C*H*OSi), 6.65 (dd, *J* = 6.9, 2.2 Hz, 1 H, C*H*NCN), 8.28 (s, 1 H, NC*H*N), 11.74 (s, 1 H, N*H*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –5.4, –5.3, –4.9, 17.9, 18.4, 22.0, 24.6, 25.6, 26.0, 43.2, 65.2, 75.9, 86.5, 89.6, 110.8, 141.4, 148.2, 153.1, 156.8, 173.6.

MS (CI): *m*/*z* (%) = 100 (100), 553 (6) [M + H^+].

HRMS: *m*/*z* [M – C_4H_9]$^+$ calcd for $C_{21}H_{36}N_5O_5Si_2$: 494.226; found: 494.226.

***N*-(9-{(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-6-oxo-6,9-dihydro-1*H*-purin-2-yl)acetamide [(*R*,*R*,*R*)-13]**

Phenyl sulfide (*R*,*R*,*S*)-**10a** (0.104 g, 0.22 mmol) was treated with tris-TMS-*N*-Ac-guanine according to GP8. After column chromatography (EtOAc), product (*R*,*R*,*R*)-**13** was obtained as colourless crystals; all analytical data correspond with those of (*S*,*S*,*S*)-**13**.

Yield: 0.046 g (37%).

9-{(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-1*H*-purin-2,6(3*H*,9*H*)-dione [(*S*,*S*,*S*)-14]

Phenyl sulfide (*S*,*S*,*R*)-**10a** (0.064 g, 0.14 mmol) was treated with tris-TMS-xanthine according to GP8. After column chromatography (EtOAc), product (*S*,*S*,*S*)-**14** was obtained as colourless crystals.

Yield: 0.054 g (76%); mp 215 °C; $[\alpha]_D^{22}$ –2.1 (*c* 1.06, $CHCl_3$); R_f = 0.7 (EtOAc).

IR (KBr): 3231, 2953, 2859, 1702, 1470, 1256, 1190, 1089, 839, 776 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.06 (s, 6 H, SiCH_3), 0.12 (s, 3 H, SiCH_3), 0.16 (s, 3 H, SiCH_3), 0.84 [s, 9 H, C(CH_3)$_3$], 0.98 [s, 9 H, C(CH_3)$_3$], 1.33 (s, 3 H, CH_3C), 2.30 (ddd, *J* = 14.4, 2.5, 2.5 Hz, 1 H, CH_2CHOSi), 3.00 (ddd, *J* = 14.4, 7.1, 5.2 Hz, 1 H, CH_2CHOSi), 3.84 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 3.97 (d, *J* = 10.2 Hz, 1 H, CH_2OSi), 4.21 (dd, *J* = 5.2, 2.5 Hz, 1 H, C*H*OSi), 6.50 (dd, *J* = 7.1, 2.5 Hz, 1 H, CH$_2$C*H*N), 8.14 (s, 1 H, NC*H*N).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.4, –5.3, –4.9, 17.9, 18.4, 22.0, 25.6, 26.0, 42.9, 65.1, 75.7, 86.6, 89.8, 105.9, 139.9, 149.5, 151.5, 155.4.

MS (CI): *m*/*z* (%) = 511 (100) [M + H^+].

HRMS: *m*/*z* [M – C_4H_9]$^+$ calcd for $C_{19}H_{33}N_4O_5Si_2$: 453.199; found: 453.199.

9-{(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-1*H*-purin-2,6(3*H*,9*H*)-dione [(*R*,*R*,*R*)-14]

Phenyl sulfide (*R*,*R*,*S*)-**10a** (0.101 g, 0.22 mmol) was treated with tris-TMS-xanthine according to GP8. After column chromatography (EtOAc), product (*R*,*R*,*R*)-**14** was obtained as colourless crystals.

Yield: 0.047 g (42%); $[\alpha]_D^{22}$ +2.2 (*c* 0.99, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**14**.

9-{(2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-6-chloro-9*H*-purine [(*S*,*S*,*S*)-15]

Phenyl sulfide (*S*,*S*,*R*)-**10a** (0.117 g, 0.25 mmol) was treated with TMS-6-chloropurine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*S*,*S*,*S*)-**15** (55%) was obtained as colourless crystals alongside (*S*,*S*,*R*)-**15** (0.036 g, 28%).

(*S*,*S*,*S*)-**15:** Yield: 0.070 g (55%); mp 122 °C; $[\alpha]_D^{21}$ +29.8 (*c* 0.85, $CHCl_3$); R_f = 0.04 (*n*-pentane–Et_2O, 1:1).

IR (KBr): 2934, 1559, 1258, 1092, 837, 776 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.02 (s, 3 H, SiC*H*$_3$), 0.98 (s, 6 H, SiC*H*$_3$), 0.12 (s, 3 H, SiC*H*$_3$), 0.84 [s, 9 H, C(C*H*$_3$)$_3$], 0.93 [s, 9 H, C(C*H*$_3$)$_3$], 1.31 (s, 3 H, C*H*$_3$C), 2.99 (ddd, *J* = 14.3, 7.4, 5.2 Hz, 1 H, C*H*$_2$CHOSi), 2.44 (ddd, *J* = 14.3, 2.5, 2.2 Hz, 1 H, C*H*$_2$CHOSi), 3.80 (d, *J* = 10.3 Hz, 1 H, C*H*$_2$OSi), 3.92 (d, *J* = 10.3 Hz, 1 H, C*H*$_2$OSi), 4.25 (dd, *J* = 5.2, 2.2 Hz, 1 H, C*H*OSi), 6.53 (dd, *J* = 7.4, 2.5 Hz, 1 H, CH$_2$C*H*N), 8.68 (s, 1 H, NC*H*NCCl), 8.74 (s, 1 H, NC*H*NCCCl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.4, –5.3, –5.2, –4.9, 18.0, 18.4, 22.0, 25.6, 26.0, 41.7, 65.3, 75.7, 83.5, 89.4, 131.7, 144.3, 150.5, 150.8, 151.5.

MS (CI): *m*/*z* (%) = 227 (100), 514 (27) [M + H$^+$].

Anal. Calcd for $C_{23}H_{41}ClN_4O_3Si_2$: C, 53.83; H, 8.05; N, 10.92. Found: C, 53.73; H, 8.03; N, 10.82.

9-{(2*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsiloxy)-5-[(*tert*-butyldimethylsiloxy)methyl]-5-methyltetrahydrofuran-2-yl}-6-chloro-9*H*-purine [(*R*,*R*,*R*)-15]

Phenyl sulfide (*R*,*R*,*S*)-**10a** (0.131 g, 0.28 mmol) was treated with TMS-6-chloropurine according to GP8. After column chromatography (*n*-pentane–Et_2O, 1:1), product (*R*,*R*,*R*)-**15** (42%) was obtained as colourless crystals alongside (*R*,*R*,*S*)-**15** (0.050 g, 35%).

(*R*,*R*,*R*)-**15**: Yield: 0.060 g (42%); $[\alpha]_D^{21}$ –31.3 (*c* 0.69, $CHCl_3$); all other analytical data correspond with those of (*S*,*S*,*S*)-**15**.

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