Direct Access to Furanosidic Eight-Membered Ulosonic Esters from *cis*-α,β-Epoxy Aldehydes

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Keywords: Aldol reactions / Cyclization / Epoxide / Regioselectivity / Ulosonic acids

Direct access to bicyclic precursors of octulosonic acids is achieved by treatment of differentially (or not) protected γ,δ-bis(silyloxy) *cis*-α,β-epoxy aldehydes with ethyl 2-(trimethylsilyloxy)-2-propenoate in the presence of boron trifluoride–diethyl ether. An X-ray crystallographic structure of a bicycle (compound **33a**) was obtained and used to determine the absolute configurations of the different stereogenic centers and thus the diastereoselective preference of the aldol reaction (*syn*) and the regioselectivity of the epoxide ring-opening (C-6 atom). Functionalization and opening of the bicyclic compound to afford octulosonic analogues in their furanoside forms was studied. An octulosonic 8-phosphate analogue has been synthesized.

Introduction

3-Deoxy-2-ulosonic acids are widespread natural compounds constituting a specific family of carbohydrates. The anomeric carbon atom is quaternary, also possessing a carboxylic functionality; in addition they are dehydroxylated in the C-3 position. Functionalized or not, these compounds participate in various important biological processes. The most important of the series (Figure 1) are 3-deoxy-D-*arabino*-2-heptulosonic acid (DAH), 3-deoxy-D-*manno*-2-octulosonic acid (KDO), 3-deoxy-D-*glycero*-D-*galacto*-2-nonulosonic acid (KDN), and 3,5-dideoxy-D-*glycero*-D-*galacto*-5-acetylamino-2-nonulosonic acid (5-NANA or sialic acid).

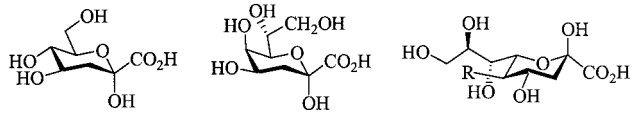

Figure 1. Most abundant natural 3-deoxy-2-ulosonic acids

DAH in its 7-phosphate form (DAH-7P) is an important intermediate in the shikimic acid pathway, by which the aromatic amino acids and a multitude of other aromatic and alicyclic compounds are biosynthesized in bacteria, fungi, and plants.[1] KDO forms a vital and unique link between the hydrophobic lipid A and the hydrophilic polysaccharide subunits in the outer membrane lipopolysaccharide (LPS) of Gram-negative bacteria. This membrane is an attractive target for the design of effective antimicrobial agents against these bacteria.[2] As incorporation of KDO appears to be a vital step in the growth of bacteria, disruption of its synthesis or incorporation into LPS can be a rational approach towards this goal.[3]

The most representative members of the KDN family are the sialic acids, usually found at the nonreducing ends of oligosaccharides, glycoproteins, and glycolipids. They are involved in the modulation of numerous biological processes such as cellular recognition signal transduction, cell adhesion, viral receptor recognition, etc.[4]

It is not surprising that these structures have evoked immense interest from both the biological and synthetic standpoints. Further study on the medicinal chemistry and biochemistry of these compounds requires practical routes to the natural and unnatural derivatives and to their analogues. Work towards the elaboration of ulosonic acids and analogues has thus accelerated and several such endeavors, including chemical, enzymatic, and chemoenzymatic syntheses, both starting from carbohydrates and de novo, have already appeared in the literature.[5–8]

Some years ago we reported a versatile synthesis of a protected DAH, starting from a non-carbohydrate precursor. The methodology was based on [4+2+1] carbon atom incorporation, starting from an α,β-epoxy aldehyde.[9] This synthesis began with a suitably chosen *trans*-α,β-epoxy aldehyde **1**, obtained from *cis*-2-butene-1,4-diol after protection, double bond isomerization, Sharpless asymmetric epoxidation, and oxidation of the alcohol. Compound **1**

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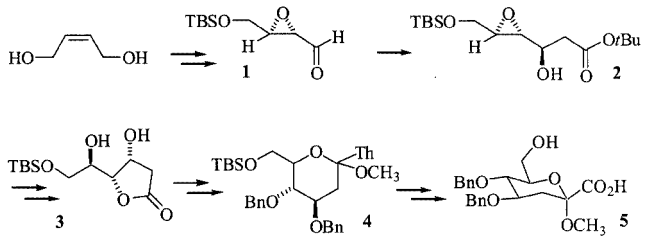
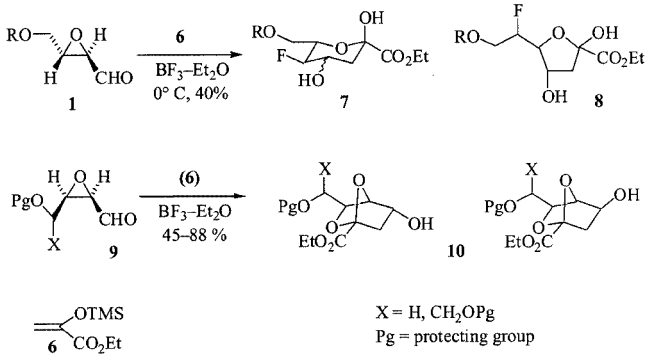
was then condensed with lithium *tert*-butyl acetate and preferentially yielded the γ,δ-epoxy-β-hydroxy ester **2** (Scheme 1).



Scheme 1

Treatment of **2** with a Lewis acid ($ZnCl_2$) quantitatively yielded hydroxybutyrolactone **3**, the result of regio- and stereocontrolled opening of the epoxide at the C-4 atom. Opening of the lactone **3** by the Weinreb method, transformation into a thiazolyl ketone, acidic protection, and benzylation of the free hydroxy groups gave compound **4**, which was then transformed into the protected heptulosonic acid **5**. Synthesis of protected DAH **5** was thus achieved in six steps (19% yield) starting from epoxy ester **2**.

Recently, while exploring a more direct route to heptulosonic analogues, we have developed a new methodology based on [4+3] carbon atom incorporation. Mukaiyama treatment of *trans*-α,β-epoxy aldehydes with ethyl 2-(trimethylsilyloxy)-2-propenoate (**6**), in the presence of the Lewis acid BF_3−diethyl ether, resulted in the direct synthesis of a separable mixture of 5- and 6-fluoroheptulosonic analogues in their pyranosidic or furanosidic forms.[10] On the other hand, when *cis*-α,β-epoxy aldehydes were employed, bicyclic precursors of ulosonic acids were obtained (Scheme 2).[11]



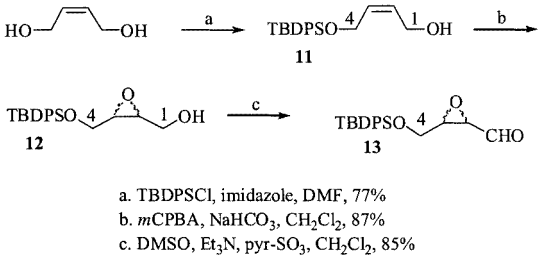
Scheme 2

As a first step in our research concerning the potential of the latter reaction, we present here a full account of the synthesis of bicyclic compounds, an interpretation of the results, functionalization, and the opening of these compounds to provide the furanosidic analogues of ulosonic acids.

Results and Discussion

Synthesis of α,β-Epoxy Aldehydes

Epoxy aldehydes **13** were prepared in three steps (monoprotection, epoxidation in the presence of *m*CPBA, and Doering oxidation of the primary alcohol, Scheme 3) and in 48% yield, starting from commercially available *cis*-2-butene-1,4-diol.

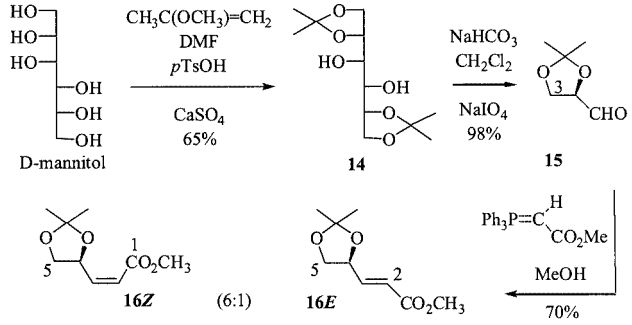


a. TBDPSCl, imidazole, DMF, 77%
b. *m*CPBA, $NaHCO_3$, CH_2Cl_2, 87%
c. DMSO, Et_3N, pyr-SO_3, CH_2Cl_2, 85%

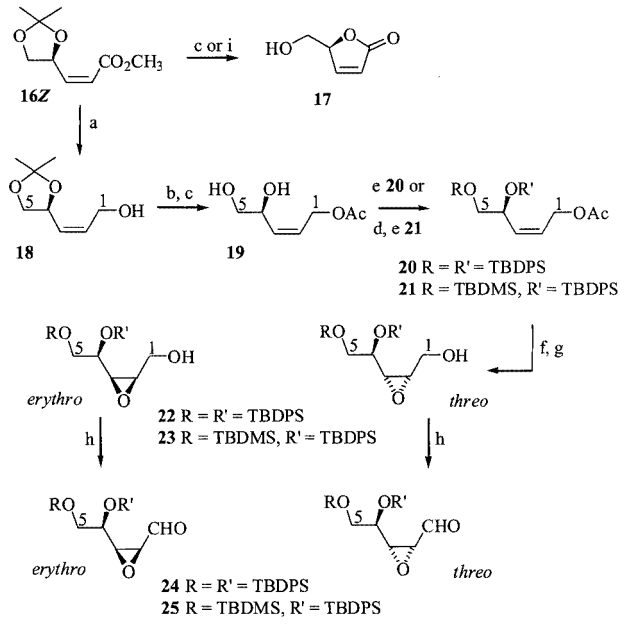
Scheme 3

Epoxy aldehydes **24** and **25** were prepared starting either from D-mannitol or from commercially available ethyl (*S*)-*cis*-4,5-*O*-isopropylidene-4,5-dihydroxy-2-pentenoate. D-Mannitol was first chosen as starting material for the preparation of *cis*-allylic alcohols containing a stereogenic center. (*R*)-Isopropylideneglyceraldehyde **15** could readily be obtained from D-mannitol in two steps (Scheme 4).[12] Treatment of D-mannitol with 2-methoxypropene in anhydrous DMF in the presence of Drierite and catalytic amounts of *p*TSA under conditions described in the literature provided a mixture of five- and six-membered acetonides. Only further treatment of this mixture in anhydrous DMF in the presence of *p*TSA (6 mmol for 100 mmol of starting D-mannitol) for 36 h at room temperature was capable of providing, through thermodynamic equilibration, 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**14**) (65%, after recrystallization). Glycol cleavage of **14** was then performed in the presence of sodium periodate by an optimized procedure described by Jackson.[13] Treatment of D-glyceraldehyde **15** with methyl (triphenylphosphoranylidene)acetate in methanol at 0 °C provided a separable mixture of the corresponding methyl esters **16*Z*** and **16*E*** in a 6:1 ratio in favor of the (*Z*) isomer and in 70% yield (Scheme 4).[14]

The *cis*-allylic alcohol **18** was synthesized either from **16*Z*** or from the commercially available ethyl ester of **16*Z***



Scheme 4



a. DIBAL-H, CH_2Cl_2, 0°C, 80% ; b. Ac_2O, Et_3N, DMAP, CH_2Cl_2, r.t., 99% ;
c. 2M HCl (aq.), CH_3CN, 0°C to r.t., 85% ; d. TBDMSCl, DMAP, CH_2Cl_2, r.t., 90% ;
e. TBDPSCl, imidazole, CH_2Cl_2, r.t., 87% ; f. KOH, CH_3OH, r.t., 92% ;
g. *m*CPBA, $NaHCO_3$, CH_2Cl_2, 0°C, 75% for **22**, 87% for **23** ;
h. Oxalyl chloride, DMSO, CH_2Cl_2, Et_3N, 90% ; i. Dowex 50x8, EtOH

Scheme 5

(Scheme 5). Attempts to eliminate the acetonide protective group first in order to introduce the silylated ones were unsuccessful; a cyclization reaction occurred to afford the butenolide **17** exclusively. This reaction was observed under all experimental conditions that might have allowed removal of the acetonide group.

Synthesis of the target alcohols was thus achieved by the following synthetic steps (Scheme 5). Reduction of the ester group in the presence of DIBAL-H gave the *cis*-allylic alcohol **18** in good yield (80%). Acetate protection of the primary hydroxy group and acetonide removal afforded diol **19** in 84% yield. The hydroxy groups could then either be identically protected (TBDPS group), furnishing compound **20**, or they could be differentiated. In the latter case, the primary hydroxy group was silylated first, by use of 1.2 equiv. of TBDMSCl in the presence of DMAP (1.8 equiv.).[15] The monoprotected compound was exclusively obtained in 87% yield. The secondary hydroxy group was then protected as a *tert*-butyldiphenylsilyl ether group (TBDPS), affording compound **21**. The epoxidation step was performed after removal of the acetate protective group (Scheme 5).

Obtention of a chiral *cis*-epoxide by the Sharpless asymmetric epoxidation reaction is difficult if not totally unfeasible, because the presence of an α chiral center in the requisite starting (*Z*)-allylic alcohol slows the epoxidation reaction considerably. Sharpless et al. have reported the lack of any reaction of the acetonide equivalent of the allylic alcohol **18** in the presence of (−)-DET, while with (+)-DET the reaction reaches only 55% completion after 14 d.[16] Alternative methods for the epoxidation of our compounds were tried, by employment of TBHP (*tert*-butyl hydroperoxide) in the presence of vanadium catalysts such as $VO(OEt)_3$ [(oxy)vanadium(v) triethoxide] or $VO(acac)_2$ [vanadium(v) acetylacetonate].[17] After 18 h, no reaction was observed when $VO(acac)_2$ was employed, while treatment with $VO(OEt)_3$ resulted in cleavage of the TBDMS protective group (after 96 h) and subsequent degradation of the epoxy alcohol.

The epoxidation reaction was therefore conducted by employing *m*CPBA at 0 °C in CH_2Cl_2 in the presence of sodium bicarbonate. After 16 h, the mixture was purified to yield the two diastereoisomers in good total yield (75% for **22** and 87% for **23**). Finally, Swern oxidation gave the desired *cis*-α,β-epoxy aldehydes **24** and **25**.

The *erythro*/*threo* diastereoselectivity in the epoxidation reaction, affording epoxy alcohols **22** and **23**, was 2:1 and 6:1, respectively, calculated by HPLC analysis. The absolute configurations of the epoxy alcohols obtained were difficult to establish at this stage. Nevertheless, characteristics of the adducts were examined by NMR spectroscopy. While ^{13}C NMR did not reveal any particular trends, ^1H NMR spectroscopy gave some helpful information. Epoxy alcohols, either those obtained here or from literature data, possessing a chiral alkoxy or silyloxy center α to the epoxide group have $J_{3/4}$ vicinal coupling constants of higher value in the *threo* series than in the *erythro* one (Figure 2).[18] A similar high value is also observed in the case of the *threo*-γ,δ-epoxy-β-(silyloxy) ester **27**, reported by us.[19]

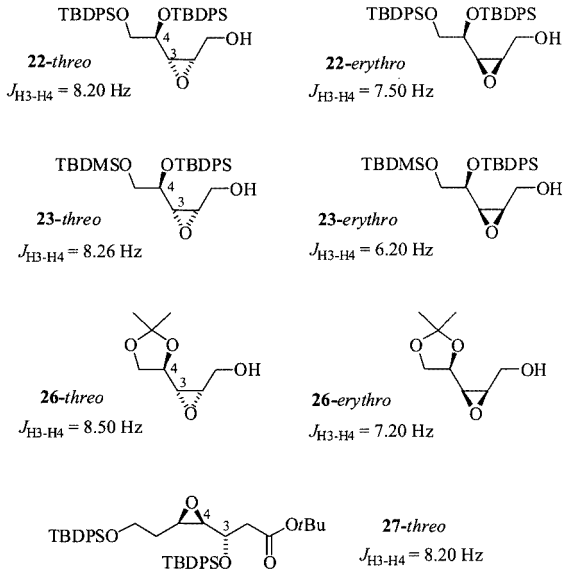
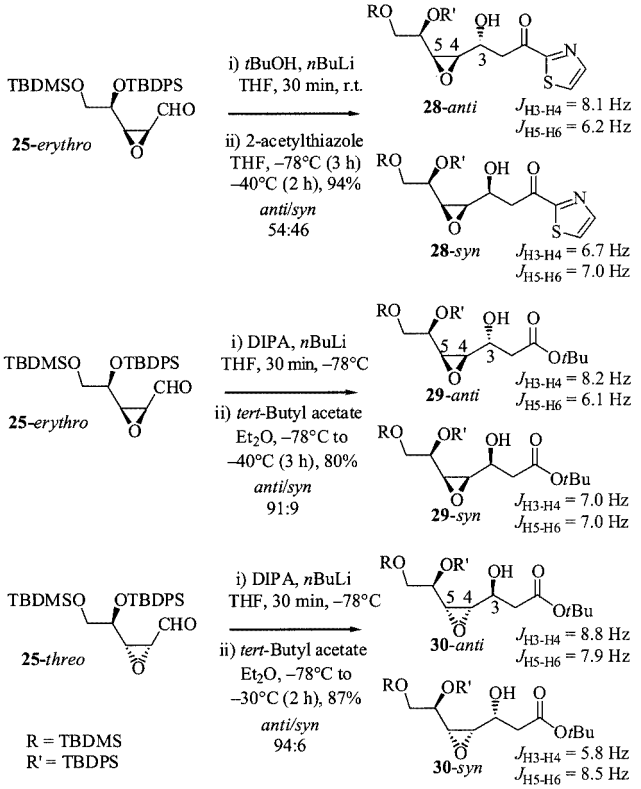


Figure 2. $J_{3/4}$ vicinal coupling constant of epoxy alcohols

In addition, aldolization products **28**−**30** were also examined by ^1H NMR spectroscopy. Compounds **28**-*anti* and **28**-*syn* were obtained from the aldol reaction between the epoxy aldehyde **25**-*erythro* and the lithium enolate of 2-acetylthiazole.[20] Compounds **29**-*anti* and **29**-*syn* were obtained from epoxy aldehyde **25**-*erythro* in aldol condensation with the lithium enolate of *tert*-butyl acetate. When the

same conditions were applied to epoxy aldehyde **25**-*threo*, compounds **30**-*anti* and **30**-*syn* were synthesized (Scheme 6).



Scheme 6

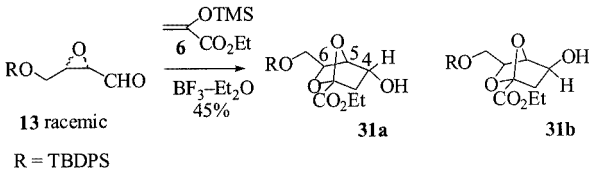
Study of the characteristics of the adducts **28**−**30** by ^{1}H NMR spectroscopy showed the same trends as before. The values of the vicinal coupling constants $J_{3/4}$ and $J_{5/6}$ were higher for an *anti* relationship between the hydroxy (or silyloxy) group and the epoxide ring than for the *syn* counterpart (Scheme 6).

The stereochemistry and absolute configurations of the epoxy alcohols were confirmed and established unambiguously after the Mukaiyama aldolization reaction, inspection of the products obtained, and an X-ray structure of one of them.

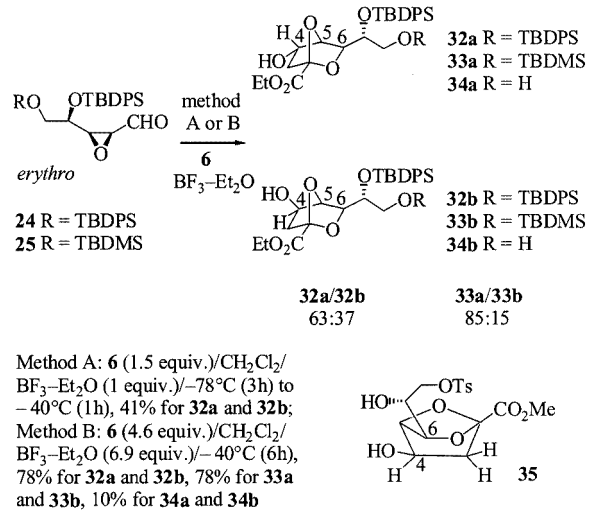
Mukaiyama Aldol Reactions

A Mukaiyama aldol condensation of α,β-epoxy aldehyde **13** was achieved with ethyl 2-(trimethylsilyloxy)-2-propenoate (**6**) in the presence of different promoters ($BiCl_3/ZnI_2$ or NaI, Eu(fod)$_3$, $LiClO_4$, Sn(OTf)$_2$, TMSOTf, BF_3−diethyl ether). Only BF_3-Et_2O gave satisfactory results and so it was used for other aldol reactions. When epoxy aldehydes **13**, **24**, and **25** were employed, bicyclic products were obtained.[11] From *cis*-α,β-epoxy aldehyde **13**, *anti* and *syn* aldolization products were formed, providing epimers **31a** and **31b** in 45% yield (Scheme 7).

Initial aldol reactions employing *erythro-cis*-α,β-epoxy aldehydes **24** afforded compounds **32a** and **32b** in 41% yield, together with 47% of recovered aldehyde (Method A,



Scheme 7



Scheme 8

Scheme 8). Gratifyingly, modification of the reaction conditions (Method B, Scheme 8) gave an improved result, and bicyclic products **32a** and **32b** were obtained in 78% yield.

This good result was also obtained when starting from *erythro-cis*-α,β-epoxy aldehyde **25** and employing these optimized conditions. Compounds **33a** and **33b** were thus obtained in 78% yield. Compounds **34a** and **34b**, resulting from removal of the TBDMS group, were also obtained, in 10% yield (total yield of 88%). If the reaction temperature reached −10 °C, adducts **34a** and **34b** were obtained as major compounds (Scheme 8).

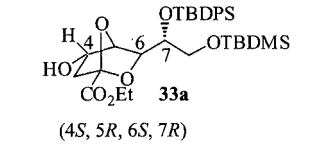
The Mukaiyama reaction was also carried out with the *threo-cis*-α,β-epoxy aldehyde diastereoisomers **24** and **25**, the corresponding bicyclic diastereoisomers of **32** and **33** also being obtained, in moderate yields (50% and 55%, respectively).

The structural assignment of the bicyclic compounds was established on the basis of NMR spectroscopy and data from the literature.[21] In fact there is only one example in the literature in which bicyclic compounds of this type were synthesized as masked octulosonic acids. Baasov's group has reported their multistep synthesis (13 steps) starting from a differentially protected arabinose derivative into which an enolpyruvate moiety had been introduced, undergoing Lewis acid intramolecular condensation. An X-ray structure of one of the synthesized bicycles was available, along with NMR spectroscopic data. According to these data there are similarities between the bicyclic frame **35** and compound **33b**: a) 3a-H resonates as a dd with $J_{3a/4a}$ = 6.41 Hz; b) 5-H (δ = 4.75 ppm) does not couple with 6-H, nor with 4-H; c) 6-H resonates at higher field (δ =

3.71 ppm) than 6-H of the isomer **33a** (δ = 4.65 ppm), as in the case of Baasov's compound.

^{1}H NMR analysis of its isomer at C-4 (**33a**) shows that 5-H (δ = 4.75 ppm) does not couple with 6-H but does couple with 4-H as a doublet with $J_{4/5}$ = 4.67 Hz.

The absolute configuration of the major bicycle adduct **33a** was determined by its X-ray structure (Figure 3). If the absolute configuration (*R*) of the C-7 atom, originating from the starting material, is taken into account, the other stereogenic centers are (*S*) (C-4), (*R*) (C-5), and (*S*) (C-6).



(4*S*, 5*R*, 6*S*, 7*R*)

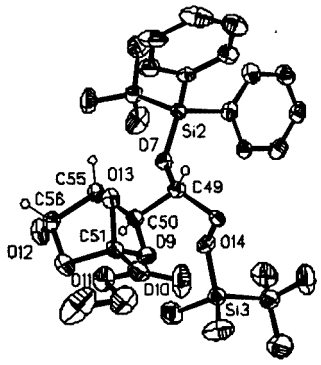
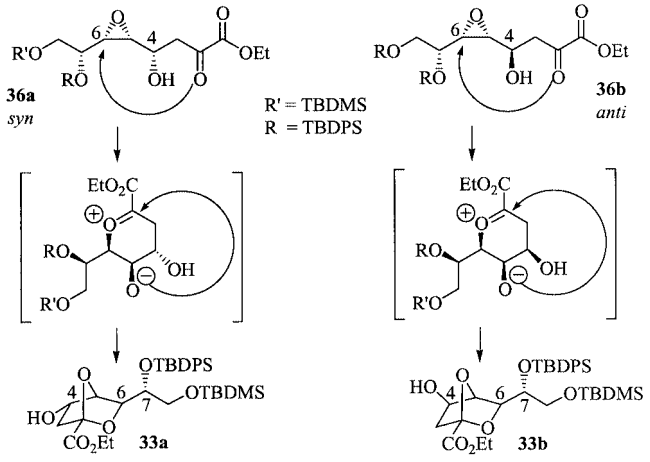


Figure 3. X-ray structure of the major bicycle adduct **33a**

Bicycle formation could be explained by the the mechanism shown in Scheme 9; firstly, a Mukaiyama aldolization reaction occurs with *syn*-diastereofacial preference to provide the intermediate γ,δ-epoxy-β-hydroxy oxo esters **36**-*anti* and **36**-*syn*, which are diastereoisomers at C-4. The cyclization process at the C-6 atom of these epoxy oxo esters can be triggered by Lewis acid mediated intramolecular attack of the carbonyl oxygen atom of the ketone on the epoxide function. Such a cyclization process would result in



Scheme 9

the formation of an oxocarbenium ion, which may react in situ with the just formed alkoxide, forming the cyclic ketal and thus the bicyclic compounds.

Aldolization reactions with different chiral α,β-epoxy aldehydes have been extensively studied in our group. In the presence of lithium ester enolates the reaction proceeds with *anti*-diastereofacial preference in all cases examined.[19] This was also the case when the α,β-epoxy aldehydes **25**-*erythro* and **25**-*threo* of this study were allowed to react with lithium *tert*-butyl acetate or lithiated acetylthiazole (Scheme 6). We have also investigated and reported the Mukaiyama aldolization reaction behavior of *cis*-α,β-epoxy aldehydes and *tert*-butyl ketene silyl acetal in the presence of various Lewis acids.[22] Again, *anti*-diastereofacial preference was observed except when an excess of $LiClO_4$ (1.5 equiv.) was used, when the poorest selectivity (*anti*/*syn* ≈ 1:1) was obtained. In that study, use of $SnCl_4$ or BF_3-Et_2O as Lewis acid catalysts was found to be unsuccessful.

In the current case, considering the C-4 epimeric bicycles, a *syn*-diastereofacial preference was observed for the Mukaiyama aldolization reaction. Even though there is no unambiguous explanation for the diastereofacial difference observed, we can invoke some points:

The same aldolization reaction with the *trans*-α,β-epoxy aldehyde analogues gave aldol compounds with *syn*-diastereofacial preference.[16]

Heathcock reported that treatment of chiral boron enolates with prochiral aldehydes can result in inversion of diastereoselectivity when catalytic or stoichiometric amounts of $SnCl_4$ are used as Lewis acid.[23] Even though we cannot compare results for catalytic and stoichiometric amounts of BF_3-Et_2O (no reaction occurred in the first case), we have also observed this effect when using $LiClO_4$, as mentioned before.

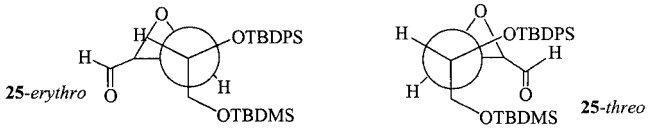
Also, in order to understand the difference in the diastereofacial preference of the Mukaiyama aldol reaction on employment of the *erythro*- and *threo*-α,β-epoxy aldehydes **25**, the energetically more favored conformers were calculated by use of the Insight II program.[24] Geometrical information and relative energies calculated for some favored conformers are reported in Table 1.

In both cases the energetically more favored conformation of the free epoxy aldehyde is the one in which the dihedral angle between the oxygen atom of the carbonyl group and that of the epoxide is ca. 170°. If it is assumed that the nucleophilic attack occurs from the face antiperiplanar to the epoxide bond, this should result in a *si* attack in the case of the *erythro* compound and a *re* attack for the *threo* aldehyde **25**, preferentially producing *syn* adducts.

We can also note that the carbonyl group of the *threo*-α,β-epoxy aldehyde is much more hindered than its counterpart in the *erythro* one. This makes the aldolization reaction more difficult and could explain the lower yield and the lower diastereoselectivity observed during the aldolization reaction of the *threo*-α,β-epoxy aldehyde **25** relative to **25**-*erythro*.

The intermediate aldol adducts **36**-*syn* and **36**-*anti* obtained were cyclized to the corresponding bicycles. The ste-

Table 1. Geometrical information and relative energies for the different conformers of compounds 25-*erythro* and 25-*threo*



	25*e* (I)	**25***e* (II)	**25***e* (III)	**25***t* (I)	**25***t* (II)	**25***t* (III)
Energy [kcal/mol]	258.57	257.40	256.31	257.00	256.72	257.60
O_{ep}−C-2−C-1−O_{ald} [°]	178	164	177	171	171	−159
O_{ep}−C-3−C-4−O_{TBDPS} [°]	56	−57	−55	−32	−32	−33
O_{ep}−C-3−C-4−C5 [°]	−67	−178	−175	−157	−157	−160

reochemistry of the products is the result of intramolecular nucleophilic attack of the oxygen atom of the carbonyl group at either C-5 or C-6 with inversion of configuration. The X-ray structure of compound **33a** unambiguously implies a 6-*endo-tet* cyclization process. This preferential opening of the epoxide ring reflects a more favorable trajectory for C-6 opening, the result of a compromise between conformational ring strain and stereochemical requirements.

Coxon et al. recently reported an ab initio study of the intramolecular ring cyclization of protonated and BF_3-coordinated *cis*-4,5-epoxyhexan-1-ol.[25] The potential energy surface for the rearrangement of protonated epoxy alcohols shows activation barriers much more favorable to five-membered transition structures leading to furan. When BF_3 is coordinated to the epoxide, on the other hand, the five-membered transition structure is marginally lower in energy than the six-membered one, so in the latter case and without consideration of any additional functional groups on the molecule, opening of the epoxide ring both at C-5 and at C-6 might occur.

For the major diastereoisomer **36**-*syn*, originating from the heavily substituted α,β-epoxy aldehyde **25**-*erythro*, cyclization at C-6 could be preferential because it would allow a better, almost antiperiplanar, stereochemical arrangement of the oxygen atoms of the epoxide ring and the 4-hydroxy group. Furthermore, in a six-membered transition state the hydroxy group originating from the aldolization reaction is almost equatorial. For the minor diastereoisomer **36**-*anti*, C-5 opening of the epoxide ring is also much less favorable because of steric hindrance between the hydroxy group at C-4 and the bulky alkylsilyloxy chain on the epoxide ring (Figure 4).

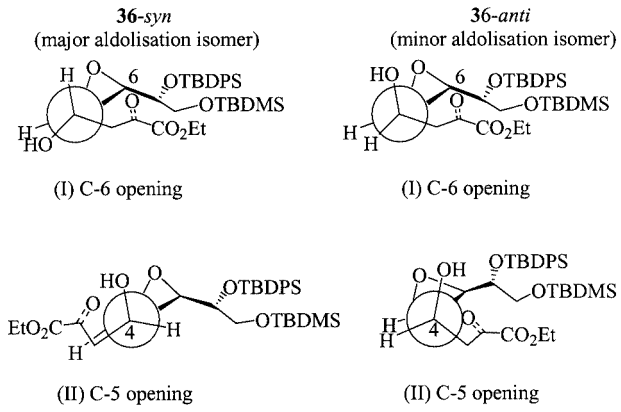


Figure 4. Energetically favored rotamers around the C-4−C-5 bond for the *syn*- and *anti*-aldol adducts

Functionalization of Bicyclic Compounds

As the synthesized bicyclic compounds **31** and **33** are masked heptulosonic and octulosonic acids, differential protection of hydroxy groups might result in different analogues of ulosonic acids.

Natural ulosonic carbohydrates are usually functionalized with phosphate or sulfate groups. In the shikimic acid pathway, for example, the natural substrate of the enzyme DHQ synthase is 3-deoxy-D-*arabino*-heptulosonic 7-phosphate (DAH, 7-P). In addition, KDO is found in its 8-phosphate form in the outer membrane lipopolysaccharide of Gram-negative bacteria.

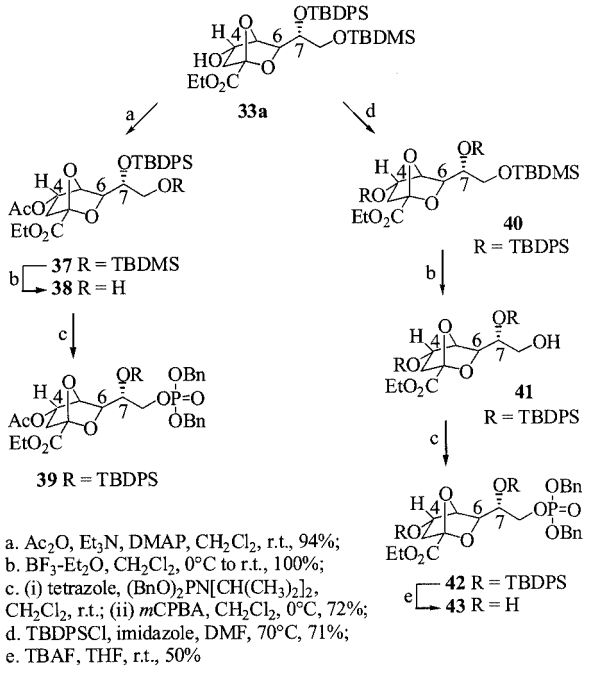
Differentiation of the primary and the secondary hydroxy group was successfully achieved in bicyclic compound **33a**. Compound **39** was synthesized by acetylation of the secondary alcohol of **33a**, selective removal of the TBDMS group, and protection of the primary alcohol as a phosphate group. In this case, all hydroxy groups have different functions (Scheme 10).

Furthermore, protection of the hydroxy group of **33a** as a TBDPS ether and selective removal of the TBDMS group gave compound **41**. Phosphorylation of the primary hydroxy group and removal of TBDPS groups provided compound **43**.

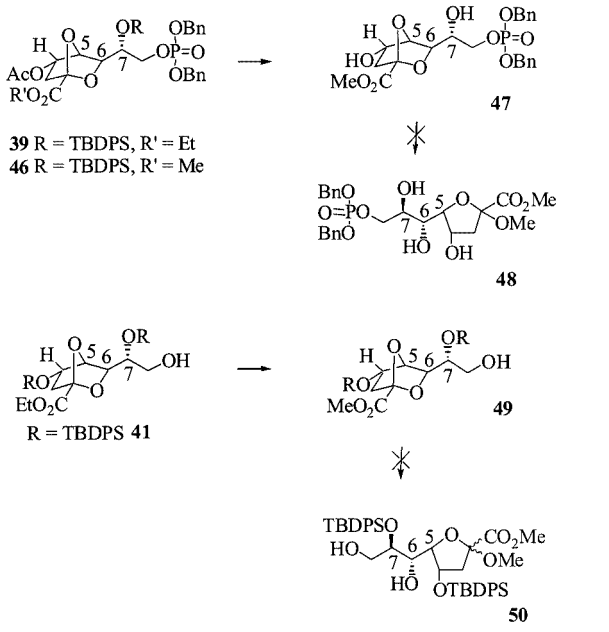
Opening of Bicyclic Compounds

In a literature report, treatment of bicyclic compound **35** with *para*-toluenesulfonic acid (*p*TsOH) in methanol induced the formation of α- and β-methyl furanoside derivatives of KDO.[21]

Starting from compound **33a**, treatment with *p*TsOH in methanol for 1 h and 45 min gave compound **44**, resulting from acidolysis of the TBDMS group and replacement of the ethyl ester group by a methyl group. Compound **44** was then subjected to the same acidic conditions, and after 16 h the α- and β-methyl furanosidic compounds **45** (analogues of the C-4 epimer of the natural compound) were



Scheme 10

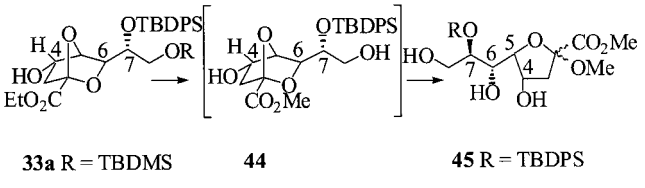


Scheme 12

obtained in 35% yield (56% based on recovered starting material). When the reaction was conducted for a longer period of time under the same conditions or the mixture was heated at 60 °C, complete loss of protective groups was observed, resulting in degradation products. Camphorsulfonic acid, a reagent with lower acidity, was then chosen. Treatment of compound **33a** for 41 h gave furanosidic compound **45** in 31% yield (60% based on recovered starting material).

The use of a Lewis acid ($SnCl_4$) in methanol was also investigated, and better results were obtained. When compound **44** was treated with $SnCl_4$ in methanol for 49 h at room temperature, the desired α- and β-methyl furanosidic compounds **45** were obtained in 62% yield (94% based on recovered starting material, Scheme 11). The TBDPS group showed better stability with $SnCl_4$ than with camphorsulfonic acid. In an attempt to reduce the reaction time, compound **44** was treated under the same conditions but with heating to 50 °C, for 15 h. Furanosidic compound **45** was obtained in 50% yield (62% based on recovered starting material).

Unfortunately, a significant decrease in reactivity was observed when employing functionalized bicyclic compounds in the acid-catalyzed opening reaction. Treatment of phosphorylated bicyclic compound **39** with *p*TsOH showed slow



Scheme 11

consumption of starting material. After 17 h, only the exchange of ethyl and methyl ester groups had been observed, giving compound **46**. This, when treated under the same conditions for 22 h, underwent removal of the acetate and TBDPS groups, affording compound **47**, which was degraded upon heating to 55 °C. Treatment of compound **39** in the presence of $SnCl_4$ in methanol for 48 h at room temperature also yielded transesterified compound **46**.

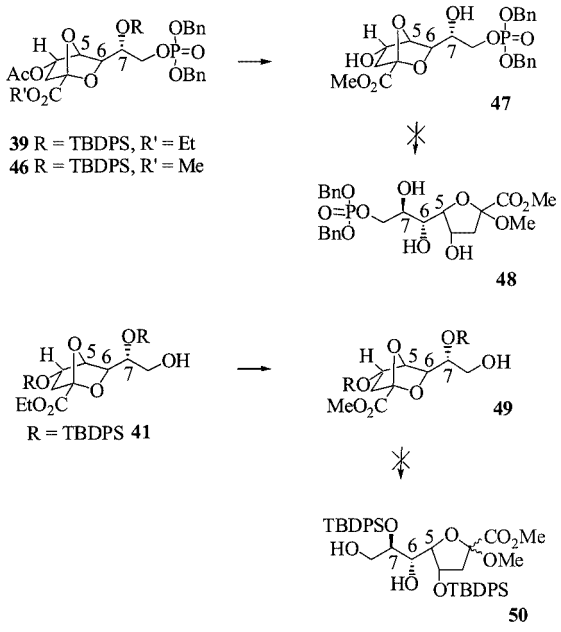
The same result was observed when compound **41**, possessing a primary hydroxy group instead of a C-4-protected one, was treated with $SnCl_4$ under conditions described before above.

Functionalization of the Primary Hydroxy Group of Furanosidic Compound 45

As described above, bicyclic compounds functionalized on the primary hydroxy group failed to react under the acid-catalyzed opening reactions. Gratifyingly, differentiation and functionalization of the hydroxy groups of furanoside compound **45** was achieved by the following reaction sequence. Selective phosphorylation at the primary hydroxy position of compound **45** was observed when triethyl phosphite and carbon tetrabromide in pyridine were used, resulting in the formation of the corresponding 8-diethylphosphate ester **51** (Scheme 13).[26]

Conclusion

In conclusion, a direct and efficient route to furanosidic eight-membered ulosonic acids is described. The aldolization reaction between the γ,δ-silyloxy *cis*-α,β-epoxy aldehydes and ethyl 2-(trimethylsilyloxy)-2-propenoate in the presence of BF_3−diethyl ether preferentially gave *syn*-aldol adducts that were cyclized in situ by an intramolecular pro-



Scheme 13

cess to provide bicycles in good to excellent yields. Functionalization and discrimination of the hydroxy groups could be achieved easily, and opening of the bicycle necessitates the presence of free primary and 4-hydroxy groups. Epimerization at the C-4 position, affording the configuration of the natural KDO, along with further functionalization will be presented in due course.

Experimental Section

General: All reactions were carried out under nitrogen. The following solvents were dried prior to use: dichloromethane (calcium hydride), diethyl ether (sodium), methanol (Mg, iodine), pyridine and triethylamine (calcium hydride and stored over potassium hydroxide pellets), and THF (sodium). TLC was performed on ALUGRAM SIL G/UV_{254} (0.2 mm) plates. Column chromatography was performed on Merck 60 silica gel (70−200 μm). Medium-pressure liquid chromatography (MPLC) was performed with a Jobin−Yvon apparatus on Merck silica (15−40 μm). High performance liquid chromatography (HPLC) was performed with PROCHROM apparatus on Merck silica (12 μm). NMR spectroscopic data were obtained with Bruker AC 200, AC 250, and AC 400 instruments operating at 200, 250, and 400 MHz (^{1}H spectra), respectively, 50, 63, and 100 MHz (^{13}C spectra), respectively, and at 161 MHz (^{31}P; AC 400). Chemical shifts are quoted in ppm downfield from tetramethylsilane, and coupling constants *J* are in Hz.[27] Infrared spectra were recorded with a Perkin−Elmer FT-IR 1725X spectrometer. Mass spectrometry data were obtained with a NERMAG R10−10 spectrometer. Elemental analyses were obtained from the microanalysis laboratory of the "Ecole Nationale Supérieure de Chimie", Toulouse, France. Optical rotations were measured with a Perkin−Elmer model 141 polarimeter.

Ethyl 2-(Trimethylsilyloxy)-2-propenoate (6): This compound was synthesized according to ref.[28]

Alcohol 11: Imidazole (15.45 g, 227 mmol) and TBDPSCl (20.8 g, 75.6 mmol) were added at room temperature to a solution of *cis*-butene-1,2-diol (6.65 g, 75.6 mmol) in dry DMF (400 mL). After the mixture had been stirred for 20 h, water (100 mL) was added and the aqueous phase was extracted with diethyl ether (800 mL). The organic phase was dried with $MgSO_4$ and filtered, and the solvent was evaporated. The oil was purified by chromatography on a silica gel column (petroleum ether/diethyl ether, 1:1, R_f = 0.3), and alcohol **11** (19 g) was obtained as a colorless oil (77% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.06 (s, 9 H, CH_3 TBDPS), 4.01 (m, 2 H, 1-H), 4.27 (m, 2 H, 4-H), 5.69−5.77 (m, 1 H, 2-H, 1 H, 3-H), 7.36−7.46 (m, 6 H, phenyl), 7.69−7.72 (m, 4 H, phenyl) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.1 (C_q, TBDPS), 26.8 (CH_3, TBDPS), 58.8, 60.3 (CH_2, C1) (CH_2, C-4), 129.6, 129.8, 129.9, 134.8, 135.8 (CH, phenyl), 130.0, 131.0 (CH, C-2, C-3), 133.4 (C_q, phenyl) ppm. $C_{20}H_{26}O_2Si$ (326.5): calcd. C 73.57, H 8.03; found C 73.44, H 8.03. IR (film): $\tilde{\nu}$ =3355 cm^{-1}, 3073, 1589, 1111.

Epoxy Alcohol 12: A solution of *m*CPBA (70% tech., 17.15 g, 69.92 mmol) in dry CH_2Cl_2 (30 mL) was added dropwise at 0 °C to a suspension of allylic alcohol **11** (11.4 g, 34.96 mmol) and $NaHCO_3$ (6.76 g, 80.42 mmol) in dry CH_2Cl_2 (250 mL). After the mixture had been stirred for 30 min at 0 °C, the ice bath was removed and the reaction mixture was stirred for a further 16 h at room temperature. Aqueous sodium bisulfite (10%, 40 mL) was added at 0 °C, and the mixture was stirred for 30 min. The organic layer was separated and washed with saturated aqueous $NaHCO_3$, dried with $MgSO_4$, and filtered, and the solvent was evaporated. The residual oil was purified by chromatography on a silica gel column (petroleum ether/ethyl acetate, 7:3, R_f = 0.33) and epoxy alcohol **12** was obtained (7.13 g, 87% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.07 (s, 9 H, CH_3, TBDPS), 2.10 (s, 1 H, OH), 3.22 (m, 1 H, 2-H, 1 H, 3-H), 3.76 (dd, $J_{3/4a}$ = 5.6, $J_{4a/4b}$ = 11.7 Hz, 1 H, 4-H), 3.91 (dd, $J_{3/4b}$ = 5.3, $J_{4a/4b}$ = 11.7 Hz, 1 H, 4-H), 7.38−7.46 (m, 6 H, phenyl), 7.66−7.71 (m, 4 H, phenyl) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.2 (C_q, TBDPS), 26.8 (CH_3, TBDPS), 56.4, 56.2 (CH, C-2) (CH, C-3), 60.8, 62.3 (CH_2, C-4) (CH_2, C-1), 127.9, 129.8, 130.0, 135.5, 135.6 (CH, phenyl), 132.9, 133.0 (C_q, phenyl) ppm. $C_{20}H_{26}O_3Si$ (342.5): calcd. C 70.13, H 7.65; found C 69.88, H 7.60. IR (film): $\tilde{\nu}$ =3421 cm^{-1}, 3073, 2935, 2861, 1470, 1100.

Aldehyde 13: Anhydrous DMSO (6 mL) and Et_3N (2.05 mL, 14.7 mmol) were added to a solution of epoxy alcohol **12** (1.0 g, 2.94 mmol) in dry dichloromethane (4.5 mL). The mixture was cooled to 0 °C, and $pyrSO_3$ complex (2.34 g, 14.7 mmol) was added in four portions. The mixture was allowed to warm to room temperature and stirred for a further 20 min. Diethyl ether (35 mL) was added, and the organic phase was washed with water (3 × 10 mL), dried with $MgSO_4$, and filtered, and the solvents were evaporated. Aldehyde **13** (845 mg) was obtained (85% yield) and employed without purification. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.07 (s, 9 H, CH_3, TBDPS), 2.76 (m, 1 H, 3-H), 2.87 (t, $J_{2/1} = J_{2/3}$ = 4.8 Hz, 1 H, 2-H), 3.53 (dd, $J_{3/4a}$ = 4.3, $J_{4a/4b}$ = 12.3 Hz, 1 H, 4-H), 3.49 (dd, $J_{3/4b}$ = 3.2, $J_{4a/4b}$ = 12.3 Hz, 1 H, 4-H), 7.18−7.23 (m, 6 H, phenyl), 7.64−7.74 (m, 4 H, phenyl) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.2 (C_q, TBDPS), 26.8 (CH_3, TBDPS), 57.8, 59.8 (CH, C-2) (CH, C-3), 60.8 (CH_2, C-4), 128.0, 130.0, 135.6 (CH, phenyl), 132.4, 132.9 (C_q, phenyl), 198.1 (C=O, CHO) ppm. MS (DCI, NH_3): *m*/*z* = 358 [M + NH_4^+]. IR (film): $\tilde{\nu}$ = 3074 cm^{-1}, 1724, 1111.

1,2,5,6-Diisopropylidene-D-mannitol (14): 2-Methoxypropene (14.4 g, 0.20 mol) and *p*TsOH (0.2 g) were successively added at 0 °C to a solution of D-mannitol (18.2 g, 0.1 mol) in anhydrous DMF (400 mL) and Drierite (1.0 g). After 2 h, further *p*TsOH (0.2 g) was added and the mixture was stirred for 1 h. 2-Methoxypropene (4 g,

0.05 mol) was then added in four portions over 2 h. Na_2CO_3 (5 g) was added and the stirring was continued for a further 1 h. The mixture was filtered and DMF was distilled. The crude product was redissolved in DMF (300 mL), *p*TsOH (1.2 g) was added, and the mixture was stirred at room temperature for 36 h. DMF was distilled off, and the residue was dissolved in dichloromethane (30 mL) and dibutyl ether (35 mL). After evaporation of dichloromethane, the desired product (11 g, 65% yield) was obtained as crystals. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (s, 6 H, CH_3, acetonide), 1.41 (s, 6 H, CH_3, acetonide), 2.63−2.66 (m, 2 H, 2 OH), 3.71−3.76 (m, 2 H), 3.94−3.99 (m, 2 H), 4.08−4.21 (m, 4 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.2, 26.7 (CH_3, acetonide), 66.8 (CH_2), 71.0, 75.8 (CH), 109.2 (C_q, acetonide) ppm.

Aldehyde 15: Saturated aqueous $NaHCO_3$ (2.7 mL) and a solution of compound **14** (6.7 g, 25.54 mmol) in dichloromethane (60 mL) were placed in a reaction vessel (250 mL) equipped with a mechanical stirrer. $NaIO_4$ (10.9 g, 51 mmol) was added, and the mixture was stirred for 1.5 h at room temperature. After decantation, dichloromethane was removed and the residue was extracted with more dichloromethane (30 mL). The solvent was evaporated and the residue was purified by distillation under reduced pressure (30 mbar, 55 °C). Pure product **15** (6.5 g) was obtained in 98% yield. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 (s, 3 H, CH_3, acetonide), 1.45 (s, 3 H, CH_3, acetonide), 4.08 (dd, $J_{3/2}$ = 4.85, $J_{3a/3b}$ = 8.73 Hz, 1 H, 3-H), 4.16 (dd, $J_{3/2}$ = 7.34, $J_{3a/3b}$ = 8.68 Hz, 1 H, 3-H), 4.37 (ddd, $J_{1/2}$ = 1.86, $J_{2/3}$ = 4.87, $J_{2/3}$ = 7.27 Hz, 1 H, 2-H), 9.70 (d, $J_{1/2}$ = 1.86 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 24.9, 26.0 (CH_3, acetonide), 65.5 (C-2), 79.6 (C-3), 111.0 (C_q, acetonide), 201.5 (C=O, CHO) ppm.

Compound 16: Methyl (trimethylphosphoranylidene)acetate (1.5 g, 4.61 mmol) was added at −10 °C to a solution of aldehyde **15** (500 mg, 3.84 mmol) in methanol (16 mL). After 20 h of stirring at −10 °C, the solvent was evaporated and the residue was redissolved in diethyl ether (10 mL). After filtration, the solvent was evaporated. The residue was then purified by chromatography on a silica gel column (petroleum ether/diethyl ether, 9:1), and compounds **16*Z*** (430 mg) and **16*E*** (70 mg) were obtained as colorless oils (70% total yield). **16*Z*:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, CH_3 acetonide), 1.44 (s, 3 H, CH_3 acetonide), 3.61 (dd, $J_{5/4}$ = 6.7, $J_{5a/5b}$ = 8.2 Hz, 1 H, 5-H), 3.70 (s, 3 H, CO_2Me), 4.37 (dd, $J_{5/4}$ = 6.9, $J_{5a/5b}$ = 8.2 Hz, 1 H, 5-H), 5.48 (dq, $J_{4/2}$ = 1.7 Hz and $J_{4/5a}$ = $J_{4/5b}$ = $J_{4/3}$ = 6.6 Hz, 1 H, 4-H), 5.85 (dd, $J_{2/4}$ = 1.7, $J_{2/3}$ = 11.6 Hz, 1 H, 2-H), 6.37 (dd, $J_{3/4}$ = 6.6, $J_{3/2}$ = 11.6 Hz, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.4 (CH_3, acetonide), 26.6 (CH_3, acetonide), 51.7 (CH_3, CO_2CH_3), 69.4 (CH_2, C-5), 73.6 (CH, C-4), 109.7 (C_q, acetonide), 120.3, 149.6 (CH, C-2 andC-3), 166.1 (C=O, CO_2CH_3) ppm. MS (DCI, NH_3): *m*/*z* = 204 [M + NH_4^+]. $C_9H_{14}O_4$ (186.1): calcd. C 58.05, H 7.58; found C 58.15, H 7.60. IR (film): $\tilde{\nu}$ =1718 cm^{-1}, 1646, 1060, 860. **16*E*:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.38 (s, 3 H, CH_3, acetonide), 1.44 (s, 3 H, CH_3, acetonide), 3.47 (s, 3 H, CO_2Me), 3.68 (dd, $J_{5/4}$ = 7.2, $J_{5a/5b}$ = 15.4 Hz, 1 H, 5-H), 4.18 (m, 1 H, 5-H), 4.65 (dq, $J_{4/2}$ = 1.4 Hz and $J_{4/5a}$ = $J_{4/5b}$ = $J_{4/3}$ = 7.0 Hz, 1 H, 4-H), 6.09 (dd, $J_{2/4}$ = 1.4, $J_{2/3}$ = 15.6 Hz, 1 H, 2-H), 6.88 (dd, $J_{3/4}$ = 5.6, $J_{3/2}$ = 15.6 Hz, 1 H, 3-H). MS (DCI, NH_3): *m*/*z* = 204 [M + NH_4^+].

5-(Hydroxymethyl)furan-2(5*H*)-one (17). Method A: Dowex (350 mg) was added to a solution of acetonide **16*Z*** (84 mg, 0.42 mmol) in ethanol (15 mL). After 8 h, the suspension was filtered and the solvent was evaporated. Compound **17** (40 mg) was obtained (83% yield). **Method B:** A solution of HCl (2 M, 0.2 mL) was added dropwise at 0 °C to a solution of acetonide (50 mg, 0.25 mmol) in acetonitrile (3.8 mL) and water (0.8 mL). After 2 h and 45 min, saturated aqueous $NaHCO_3$ was added, and the aqueous phase was extracted with CH_2Cl_2 and ethyl acetate. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated, to provide compound **17** (24 mg, 84% yield) (ethyl acetate/methanol, 95:5, R_f = 0.54). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.52, 3.65 (2 dd, $J_{5a/4}$ = 4.0, $J_{5b/4}$ = 4.86, $J_{5a/5b}$ = 12.1 Hz, 1 H, 5-H), 4.90 (t, $J_{3/4}$ = 1.50, $J_{4/2}$ = 2.04 Hz, 1 H, 4-H), 5.88 (dd, $J_{3/2}$ = 5.76 Hz and $J_{4/2}$ = 2.04 Hz, 1 H, 2-H), 7.34 (dd, $J_{3/2}$ = 5.76, $J_{3/4}$ = 1.50 Hz, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 61.6 (CH_2, C-5), 84.3 (CH, C-4), 122.0 (CH, C-3), 154.7 (CH, C-2), 173.4 (C=O) ppm. MS (DCI, NH_3): *m*/*z* = 115 [M + H^+], 132 [M + NH_4^+]. $C_5H_6O_3$ (114.1): calcd. C 52.63, H 5.30; found C 52.69, H 5.35. IR (film): $\tilde{\nu}$ =3416 cm^{-1}, 1737, 1602.

Alcohol 18: DIBAL-H (1 M in CH_2Cl_2, 28.0 mmol, 28.0 mL) was slowly added at 0 °C to a solution of ethyl (2*Z*,3*S*)-(+)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propenoate (3.04 g, 15.2 mmol) in dry CH_2Cl_2 (80 mL). The solution was stirred for 4 h at 0 °C. A saturated aqueous ammonium chloride solution (10 mL) was then added, and the mixture was stirred at room temperature for a further 30 min. After filtration, the organic phase was washed with water, dried with $MgSO_4$, and filtered, and the solvent was evaporated. The oil was purified by chromatography on a silica gel column (petroleum ether/diethyl ether, 7:3 to 3:7) (petroleum ether/diethyl ether, 3:7, R_f = 0.30) to give the desired product (1.92 g, 80% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.39 (s, 3 H, CH_3, acetonide), 1.45 (s, 3 H, CH_3, acetonide), 3.56 (t, *J* = 8.0 Hz, 1 H, 5-H), 4.09 (dd, *J* = 6.2 Hz and *J* = 8.1 Hz, 1 H, 5-H), 4.21−4.29 (m, 2 H, 1-H), 4.87 (q, *J* = 7.0 Hz, 1 H, 4-H), 5.56 (t, *J* = 8.1 Hz, 1 H, 3-H), 5.79−5.86 (m, 1 H, 2-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 25.9 (CH_3, acetonide), 26.7 (CH_3, acetonide), 58.7 (CH_2, C-1), 69.6 (CH_2, C-5), 71.9 (CH, C-4), 109.5 (C_q, acetonide), 129.6, 133.1 (CH, C-2 andC-3) ppm. MS (DCI, NH_3): *m*/*z* = 159 [M + H^+], 176 [M + NH_4^+]. IR (film): $\tilde{\nu}$ =3412 cm^{-1}, 1651, 1059, 859. $C_8H_{14}O_3$ (158.1): calcd. C 60.74, H 8.92; found C 60.88, H 8.90.

Acetate 19: Et_3N (3.0 mL), Ac_2O (1.5 mL), and DMAP (20 mg, 0.16 mmol) were added at room temperature to a solution of alcohol **18** (403 mg, 2.55 mmol) in dry CH_2Cl_2 (20 mL). The mixture was stirred for 1 h at room temperature and washed with saturated aqueous $NaHCO_3$, and the organic phase was dried with $MgSO_4$, filtered, and concentrated. The oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 1:1, R_f = 0.46), and the desired acetate (510 mg, 99% yield) was obtained. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, acetonide), 1.40 (s, 3 H, acetonide), 2.03 (s, 3 H, OAc), 3.54 (t, $J_{5a/5b}$ = 7.9 Hz, 1 H, 5-H), 4.08 (dd, $J_{4/5}$ = 6.4, $J_{5a/5b}$ = 7.9 Hz, 1 H, 5-H), 4.62−4.66 (m, 2 H, 1-H), 4.84 (ddd, *J* = 7.6, *J* = 7.0, *J* = 6.4 Hz, 1 H, 4-H), 5.58−5.72 (m, 1 H, 2-H, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.9 (CH_3, OAc), 25.6 (CH_3, acetonide), 26.6 (CH_3, acetonide), 60.0 (CH_2, C-1), 69.3 (CH_2, C-5), 71.8 (CH, C-4), 109.5 (C_q, acetonide), 127.6, 132.0 (CH, C-2 and C-3), 170.7 (C=O, OAc) ppm. MS (DCI, NH_3): *m*/*z* = 201 [M + H^+], 218 [M + NH_4^+]. IR (film): $\tilde{\nu}$ =2988 cm^{-1}, 2874, 1741, 1649, 1456, 1376, 1230, 1157, 1060, 1032, 966, 859. HCl (2 M, 0.4 mL) was added dropwise at 0 °C to a solution of acetonide (64 mg, 0.32 mmol) in acetonitrile (3.8 mL) and water (0.8 mL). After 2 h and 30 min, saturated aqueous $NaHCO_3$ was added and the aqueous phase was extracted with CH_2Cl_2 and ethyl acetate. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/ethyl acetate,10:90, R_f = 0.23), and diol **19** (44 mg, 85% yield) was obtained. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.05 (s, 3 H, OAc), 3.49 (dd, $J_{5/4}$ = 7.33, $J_{5a/5b}$ = 11.29 Hz, 1 H, 5-H), 3.57 (dd, $J_{4/5}$ = 3.97,

$J_{5a/5b}$ = 11.29 Hz, 1 H, 5-H), 4.58 (dd, J = 3.97, J = 8.24 Hz, 2 H, 1-H), 4.78 (dd, J = 6.41, J = 13.13 Hz, 1 H, 4-H), 5.61−5.65 (m, 1 H, 2-H, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.0 (CH_3, OAc), 58.5 (CH_2, C-1), 66.0 (CH_2, C-5), 68.6 (CH, C-4), 127.0, 132.9 (CH, C-2 and C-3), 171.4 (C=O, OAc) ppm. MS (DCI, NH_3): m/z = 143 [M + H$^+$ − H_2O], 161 [M + H$^+$], 178 [M + NH_4^+]. IR (film): ṽ =3401 cm^{-1}, 3030, 2932, 2872, 1738, 1656, 1427, 1375, 1239, 1071, 1031, 958, 873.

Compound 20: A solution of TBDPSCl (2.71 g, 9.9 mmol) in CH_2Cl_2 (10 mL) was slowly added at room temperature to a solution of diol **19** (720 mg, 4.5 mmol) and imidazole (1.34 g, 19.8 mmol) in CH_2Cl_2 (15 mL). The reaction mixture was stirred for 2 h at room temperature. Water (20 mL) was added, and the organic phase was washed with saturated aqueous $NaHCO_3$ (10 mL), dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 90:10, R_f = 0.56), and the desired product (2.0 g, 70% yield) was obtained. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.99 (s, 9 H, *t*Bu, OTBDMS), 1.03 (s, 9 H, *t*Bu, OTBDMS), 1.95 (s, 3 H, OAc), 3.49 (dd, $J_{5/4}$ = 5.90, $J_{5a/5b}$ = 10.00 Hz, 1 H, 5-H), 3.67 (dd, $J_{5/4}$ = 5.40, $J_{5a/5b}$ = 10.00 Hz, 1 H, 5-H), 4.03−4.20 (m, 2 H, 1-H), 4.48−4.56 (m, 1 H, 4-H), 5.30−5.46 (m, 1 H, 3-H), 5.57−5.65 (m, 1 H, 2-H), 7.26−7.57 (m, 12 H, phenyl), 7.58−7.68 (m, 8 H, phenyl) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.10 and 19.20 (C_q, *t*Bu), 20.90 (CH_3, OAc), 26.70 and 26.90 (CH_3, *t*Bu), 60.60 (CH_2, C-1), 67.90 (CH_2, C-5), 70.30 (CH, C-4), 127.50 (CH, C-2), 129.60 (CH, C-3), 133.80 and 134.60 (C_q, TBDPS), 135.60, 135.80, 136.00 (CH, phenyl), 170.80 (C=O, OAc) ppm. MS (DCI, NH_3): m/z = 654 [M + NH_4^+]. $[\alpha]_D^{25}$ = −5.8 (c = 0.7, $CHCl_3$). IR (film): ṽ =3071 cm^{-1} (C=CH aromatic), 1743 (C=O), 1472 (C=C aromatic), 1428, 1373.

Compound 21: A solution of TBDMSCl (420 mg, 2.80 mmol) in dry CH_2Cl_2 (5 mL) was slowly added at room temperature to a solution of diol **19** (366 mg, 2.28 mmol) and DMAP (510 mg, 4.18 mmol) in dry CH_2Cl_2 (13 mL). The solution was stirred for 5 h. The organic phase was washed with a saturated solution of NaCl, dried with $MgSO_4$, filtered, and concentrated. The oil was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 7:3, R_f = 0.56), and the TBDMS ether product (562 mg, 90% yield) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, CH_3, OTBDMS), 0.92 (s, 9 H, *t*Bu, OTBDMS), 2.07 (s, 3 H, OAc), 3.49 (dd, $J_{5/4}$ = 7.55, $J_{5a/5b}$ = 9.99 Hz, 1 H, 5-H), 3.61 (dd, $J_{5/4}$ = 4.18, $J_{5a/5b}$ = 9.99 Hz, 1 H, 5-H), 4.48−4.54 (m, 1 H, 4-H), 4.64−4.70 (m, 1 H, 1-H), 4.72−4.77 (m, 1 H, 1-H), 5.56−5.61 (m, 1 H, 3-H), 5.64−5.71 (m, 1 H, 2-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.20 (CH_3, TBDMS), −5.13 (CH_3, TBDMS), 18.3 (C_q, *t*Bu), 21.14 (CH_3, OAc), 26.06 (CH_3, *t*Bu), 60.71 (CH_2, C-1), 66.79 (CH_2, C-5), 68.69 (CH, C-4), 127.27 (CH, C-2), 132.94 (CH, C-3), 170.90 (C=O, OAc) ppm. MS (DCI, NH_3): m/z = 257 [M + H$^+$ − H_2O], 275 [M + H$^+$], 292 [M + NH_4^+]. A solution of TBDPSCl (331 mg, 1.20 mmol) in CH_2Cl_2 (3 mL) was slowly added at room temperature to a solution of monoprotected alcohol (166 mg, 0.60 mmol) and imidazole (100 mg, 1.45 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred for 2 h and 15 min at room temperature. Water (5 mL) was added, and the organic phase was washed with saturated aqueous $NaHCO_3$ (5 mL), dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 95:5, R_f = 0.56), affording the desired product (270 mg, 87% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.05 (s, 3 H, CH_3, OTBDMS), −0.04 (s, 3 H, CH_3, OTBDMS), 0.82 and 1.07 (s, 9 H each singlet, *t*Bu, OTBDMS, *t*Bu, TBDPS), 2.04 (s, 3 H, OAc), 3.43 (dd, $J_{5/4}$ = 7.01, $J_{5a/5b}$ = 9.77 Hz, 1 H, 5-H), 3.59 (dd, $J_{5/4}$ = 5.19, $J_{5a/5b}$ = 9.77 Hz, 1 H, 5-H), 4.10−4.30 (m, 2 H, 1-H), 4.35−4.50 (m, 1 H, 4-H), 5.40−5.60 (m, 1 H, 2-H, 1 H, 3-H), 7.34−7.42 (m, 4 H, CH C_6H_5), 7.62−7.70 (m, 6 H, CH, C_6H_5) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.37 (CH_3, TBDMS), 18.40 (C_q, *t*Bu), 19.29 (C_q, *t*Bu), 20.95 (CH_3, OAc), 25.96 (CH_3, *t*Bu), 60.80 (CH_2, C-1), 67.21 (CH_2, C-5), 70.38 (CH, C-4), 125.23, 127.52, 127.63, 129.66, 129.71, 134.67, 135.97 (CH, C-2, CH, C-3, CH aromatic), 133.85, 133.92 (C_q, aromatic), 170.65 (C=O, OAc) ppm. MS (DCI, NH_3): m/z = 530 [M + NH_4^+].

Compounds 22-*erythro* and 22-*threo*: The same experimental procedure as described for the synthesis of compounds **23** was applied, starting from the corresponding allylic alcohol (1.0 g, 1.68 mmol; 765 mg of products **22**, 75% yield). The diastereoisomers (*dr* 66:34) were separated by HPLC (silica, eluent petroleum ether/diethyl ether, 7:3). **22-*erythro*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05, 1.08 (s, 18 H, *t*Bu, TBDPS), 2.90 (ddd, $J_{2/3}$ = 3.8, J = 7.0 Hz, 1 H, 2-H), 2.95−2.99 (m, 1 H, 1-H), 3.05−3.09 (m, 1 H, 1-H), 3.23 (dd, $J_{3/4}$ = 7.5, $J_{2/3}$ = 3.9 Hz, 1 H, 3-H), 3.64 (ddd, $J_{4/5a}$ = 4.4, $J_{4/5b}$ = 3.2, $J_{3/4}$ = 7.5 Hz, 1 H, 4-H), 3.74 (2dd, $J_{5a/5b}$ = 10.7, $J_{5a/4}$ = 4.4, $J_{5b/4}$ = 3.2 Hz, 2 H, 5-H), 7.26−7.68 (m, 20 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3 (C_q, *t*Bu), 26.90 (CH_3, *t*Bu), 57.20 (CH, C-2), 57.40 (CH, C-3), 60.40 (CH_2, C-1), 66.90 (CH_2, C-5), 70.60 (CH, C-4), 127.80, 129.70, 135.90, 136.10 (CH, C_6H_5), 133.30, 133.60 (C_q, C_6H_5) ppm. $[\alpha]_D^{25}$ = −5.1 (c = 0.9, $CHCl_3$) ppm. $C_{37}H_{46}O_4Si_2$ (610.9): calcd. C 72.74, H 7.59; found C 72.62, H 7.51. IR (film): ṽ =3436 cm^{-1}, 3072, 3050, 2955, 2031, 2895, 2858, 1590, 1473, 1463, 1428, 1391, 1362, 1335, 1257, 1217, 1189, 1047, 1005, 969, 922, 869, 837, 776, 760, 741, 703, 668. **22-*threo*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99, 1.05 (s, 18 H, *t*Bu, TBDPS), 3.10 (dd, $J_{2/3}$ = 4.40, $J_{2/1}$ = 5.10 Hz, 1 H, 2-H), 3.16 (dd, $J_{2/3}$ = 4.40, $J_{3/4}$ = 8.20 Hz, 1 H, 3-H), 3.30−3.31 (m, 2 H, 1-H), 3.57 (2 dd, $J_{5a/5b}$ = 10.3, $J_{5a/4}$ = 4.70, $J_{5b/4}$ = 7.0 Hz, 2 H, 5-H), 3.63 (m, 1 H, 4-H), 7.26−7.69 (m, 20 H, C_6H_5) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.20 (C_q, *t*Bu), 19.40 (C_q, *t*Bu), 26.90 (CH_3, *t*Bu), 56.90 (CH, C-2), 59.80 (CH, C-3), 60.90 (CH_2, C-1), 66.40 (CH_2, C-5), 72.40 (CH, C-4), 127.50, 129.70, 135.70, 135.90, 136.10 (CH, C_6H_5), 133.20, 133.90 (C_q, C_6H_5) ppm. $[\alpha]_D^{25}$ = −14.8 (c = 0.9, $CHCl_3$).

Compounds 23-*erythro* and 23-*threo*: KOH (100 mg, 1.78 mmol) was added at room temperature to a solution of acetate **21** (269 mg, 0.52 mmol) in dry methanol (15 mL). After 30 min of stirring, the solvent was evaporated. The oil was dissolved in CH_2Cl_2 (15 mL) and washed with water (2 × 5 mL), dried with $MgSO_4$, and filtered, and the solvent was evaporated. The desired product (225 mg, 92% yield) was obtained and employed without purification (petroleum ether/ethyl acetate, 9:1, R_f = 0.44). ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.01 (s, 3 H, CH_3, OTBDMS), −0.00 (s, 3 H, CH_3, OTBDMS), 0.85 and 1.07 (s, 9 H, *t*Bu, OTBDPS, *t*Bu, OTBDMS), 3.40 (dd, $J_{5/4}$ = 8.24, $J_{5a/5b}$ = 9.46 Hz, 1 H, 5-H), 3.60−3.75 (m, 1 H, 5-H, 2 H, 1-H), 4.51 (ddd, J = 5.19, J = 8.54, J = 10.98 Hz, 1 H, 4-H), 5.45−5.65 (m, 1 H, 2-H, 1 H, 3-H), 7.34−7.42 (m, 4 H, CH, C_6H_5), 7.62−7.70 (m, 6 H, CH, C_6H_5) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.37 (CH_3, TBDMS), 18.56 and 19.26 (C_q, *t*Bu, TBDMS, TBDPS), 26.01 and 26.97 (CH_3, *t*Bu, TBDMS, TBDPS), 58.14 (CH_2, C-1), 66.75 (CH_2, C-5), 69.87 (CH, C-4), 125.23, 127.53, 127.67, 129.78, 129.82, 130.42, 134.15, 135.89, 136.04 (CH, C-2, CH, C-3, CH aromatic), 133.86 (C_q, aromatic) ppm. A solution of *m*CPBA (165 mg, 0.67 mmol) in dry CH_2Cl_2 (7 mL) was added dropwise at 0 °C to a suspension of allylic alcohol (166 mg, 0.35 mmol) and $NaHCO_3$ (140 mg, 1.65 mmol) in dry CH_2Cl_2 (5 mL). After the mixture had been stirred at 0 °C for 30

min, the ice bath was removed and the reaction mixture was stirred for a further 16 h at room temperature. Aqueous sodium bisulfite (10%, 10 mL) was added at 0 °C, and the mixture was stirred for 30 min. The organic layer was separated and washed with saturated aqueous $NaHCO_3$, dried with $MgSO_4$, and filtered, and the solvent was evaporated. The residual oil was purified by chromatography on a silica gel column (petroleum ether/diethyl ether, 6:4) and the epoxy alcohol (150 mg, 87% yield) was obtained. The diastereoisomers (*dr*, 86:14) were separated by HPLC (silica, petroleum ether/M0, 70:30, M0 = CH_2Cl_2/ethyl acetate, 80:20, R_f of minor isomer = 0.26 and R_f of major isomer = 0.15). **23-*erythro*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.04, −0.06 (CH_3, TBDMS), 0.92, 1.07 (*t*Bu, TBDMS, TBDPS), 1.50−1.60 (m, 1 H, OH), 3.03 (dt, $J_{2/3}$ = 4.18, J = 6.9 Hz, 1 H, 2-H), 3.15 (dd, $J_{3/4}$ = 6.2, $J_{2/3}$ = 4.18 Hz, 1 H, 3-H), 3.18 −3.27 (m, 1 H, 1-H), 3.28 −3.38 (m, 1 H, 1-H), 3.64−3.66 (m, 2 H, 5-H, 1 H, 4-H), 7.34−7.42 (m, 6 H, C_6H_5), 7.67−7.71 (m, 4 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.35 (CH_3, TBDMS), −5.23 (CH_3, TBDMS), 18.64 (C_q, *t*Bu), 19.50 (C_q, *t*Bu), 26.15 (CH_3, *t*Bu), 27.00 (CH_3, *t*Bu), 57.19 (CH, C-2), 57.44 (CH, C-3), 60.77 (CH_2, C-1), 66.23 (CH_2, C-5), 71.11 (CH, C-4), 127.91, 127.94, 130.12, 130.21, 136.10, 136.14 (CH, C_6H_5), 133.46, 133.70 (C_q, C_6H_5) ppm. MS (DCI, NH_3): *m*/*z* = 487 [M + H$^+$], 504 [M + NH_4^+]. $C_{27}H_{42}O_4Si_2$ (486.8): calcd. C 66.62, H 8.70; found C 66.85, H 8.63. IR (film): ṽ = 3436 cm^{-1}, 3072, 3050, 2955, 2031, 2895, 2858, 1590, 1472, 1463, 1428, 1390, 1362, 1335, 1257, 1217, 1189, 1047, 1005, 969, 922, 871, 837, 778, 760, 741, 703, 668. $[\alpha]_D^{25}$ = −22.02 (*c* = 1.09, $CHCl_3$). **23-*threo*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.02, −0.00 (CH_3, TBDMS), 0.83, 1.12 (*t*Bu, TBDMS, TBDPS), 2.68−2.71 (m, 1 H, OH), 3.11 (dd, $J_{2/3}$ = 4.13, $J_{3/4}$ = 8.26 Hz, 1 H, 3-H), 3.18−3.27 (m, 1 H, 2-H, 1 H, 1-H), 3.49−3.71 (m, 2 H, 5-H, 1 H, 4-H, 1 H, 1-H), 7.34−7.42 (m, 6 H, C_6H_5), 7.67−7.71 (m, 4 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.49 (CH_3, TBDMS), −5.38 (CH_3, TBDMS), 19.50 (C_q, *t*Bu), 19.50 (C_q, *t*Bu), 26.17 (CH_3, *t*Bu), 27.12 (CH_3, *t*Bu), 56.18 (CH, C-2), 59.97 (CH, C-3), 61.09 (CH_2, C-1), 65.55 (CH_2, C-5), 72.03 (CH, C-4), 127.74, 127.87, 129.85, 130.04, 130.08, 135.02, 136.09, 136.24 (CH, C_6H_5), 133.31, 134.02 (C_q, C_6H_5). MS (DCI, NH_3): *m*/*z* = 487 [M + H$^+$], 504 [M + NH_4^+]. IR (film): ṽ = 3436 cm^{-1}, 3072, 3050, 2955, 2031, 2895, 2858, 1590, 1472, 1463, 1428, 1390, 1362, 1335, 1257, 1217, 1189, 1047, 1005, 969, 922, 871, 837, 778, 760, 741, 703, 668. $[\alpha]_D^{25}$ = −15.24 (*c* = 2.31, $CHCl_3$).

Aldehydes 24-*erythro* and 24-*threo*: These compounds were prepared in the same way as compound **25**-*erythro*, starting from epoxy alcohol **22**-*erythro* (546 mg, 0.90 mmol) and **22**-*threo* (44 mg, 0.07 mmol), respectively. Aldehydes **24**-*erythro* (493 mg, 90% yield) and aldehyde **24**-*threo* (42 mg, 99% yield) were obtained. **24-*erythro*:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.00, 1.09 (s, 18 H, *t*Bu, TBDPS), 3.27 (t, J = 5.60 Hz, 1 H, 2-H), 3.55−3.62 (m, 2 H, 5-H, 1 H, 3-H), 3.99 (q, J = 5.20 Hz, 1 H, 4-H), 7.25−7.44 (m, 12 H, C_6H_5), 7.50−7.66 (m, 8 H, C_6H_5), 9.17 (d, J = 5.50 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.2 (C_q, *t*Bu), 26.9 and 26.8 (CH_3, *t*Bu), 57.7 (CH), 60.7 (CH), 66.1 (CH_2, C-5), 69.5 (CH, C-4), 127.7, 129.9, 135.5, 135.7, 135.9 (CH, C_6H_5), 132.7, 133.0 (C_q, C_6H_5), 197.7 (CHO) ppm. $[\alpha]_D^{25}$ = −10.2 (*c* = 0.5, $CHCl_3$). IR (film): ṽ = 3072 cm^{-1}, 2930, 2858, 1722, 1590, 1473, 1428, 1391, 1362, 1257. 1112, 1005, 837, 780. **24-*threo*:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.97, 1.07 (s, 18 H, *t*Bu, TBDPS), 3.32 (t, J = 5.50 Hz, 1 H, 2-H), 3.50−3.70 (m, 2 H, 5-H, 1 H, 3-H), 3.75−3.90 (m, 1 H, 4-H), 7.28−7.71 (m, 20 H, C_6H_5), 8.85 (d, J = 5.80 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.0 (C_q, *t*Bu), 26.7 and 26.9 (CH_3, *t*Bu), 58.2 (CH), 61.4 (CH), 65.6 (CH_2, C-5), 71.5 (CH, C-4), 127.7, 129.9, 135.5, 136.0, 136.2 (CH, C_6H_5), 132.8, 133.3 (C_q, C_6H_5), 197.0 (CHO) ppm.

Aldehyde 25-*erythro*: DMSO (4.23 mmol, 300 μL) was added at −78 °C to a solution of oxalyl chloride (2.11 mmol, 183 μL) in CH_2Cl_2 (2 mL), and the mixture was stirred for 10 min. Epoxy alcohol **23**-*erythro* (0.52 mmol, 257 mg) in CH_2Cl_2 (7 mL) was then added, and the resulting solution was stirred for 1 h at the same temperature. Et_3N (6.33 mmol, 0.88 mL) was then added at room temperature, followed 15 min later by water (5 mL), and the mixture was stirred for a further 10 min. The organic phase was washed with a saturated solution of $NaHCO_3$, dried with $MgSO_4$, and filtered, and the solvent was evaporated. The oil was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 9:1, R_f = 0.55) and the aldehyde (231 mg, 90% yield) was obtained. ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.13, −0.07 (CH_3, TBDMS), 0.81, 1.05 (*t*Bu, TBDMS, TBDPS), 3.31 (t, J = 4.57 Hz, 1 H), 3.45−3.52 (m, 3 H), 4.01 (q, J = 4.57 Hz, 1 H), 7.35−7.47 (m, 6 H, C_6H_5), 7.64−7.72 (m, 4 H, C_6H_5), 9.41 (d, J = 4.61 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.2 (C_q, *t*Bu), 19.2 (C_q, *t*Bu), 25.8 (CH3, *t*Bu), 26.9 (CH_3, *t*Bu), 57.7 (CH), 60.6 (CH), 65.0 (CH_2, C-5), 69.5 (CH, C-4), 127.8, 135.6, 135.9 (CH, C_6H_5), 130.1, 132.6 (C_q, C_6H_5), 198.3 (CHO) ppm. MS (DCI, NH_3): *m*/*z* = 485 [M + H$^+$], 502 [M + NH_4^+]. IR (film): ṽ = 3073 cm^{-1}, 2930, 2858, 1722, 1590, 1472, 1391, 1362, 1257. 1112, 1005, 837.

Aldehyde 25-*threo*: This compound was prepared in the same way as isomer **25**-*erythro*, starting from epoxy alcohol **23**-*threo* (100 mg, 0.20 mmol; 95 mg of aldehyde **25**-*threo*, 95% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.14, −0.12 (CH_3, TBDMS), 0.76, 1.10 (*t*Bu, TBDMS, TBDPS), 3.32−3.57 (m, 4 H), 3.70−3.79 (m, 1 H), 7.38−7.44 (m, 6 H, C_6H_5), 7.67−7.74 (m, 4 H, C_6H_5), 8.88 (d, J = 5.80 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.3 (C_q, *t*Bu), 25.9 (CH_3, *t*Bu), 26.9 (CH_3, *t*Bu), 58.1 (CH), 61.4 (CH), 64.5 (CH_2, C-5), 71.8 (CH, C-4), 127.7, 135.8, 135.9 (CH, C_6H_5), 132.6, 133.5 (C_q, C_6H_5), 196.7 (CHO) ppm. MS (DCI, NH_3): *m*/*z* = 485 [M + H$^+$], 502 [M + NH_4^+].

Compound 28: A solution of *n*BuLi (1.6 M in hexane, 240 μL, 0.384 mmol) was added at room temperature to a solution of *tert*-butyl alcohol (23 mg, 0.314 mmol) in dry THF (2 mL). After the mixture had been stirred for 30 min, it was cooled to −78 °C and a solution of aldehyde **25**-*erythro* (160 mg, 0.314 mmol) and 2-acetylthiazole (48 mg, 0.378 mmol) in dry THF (6 mL) was slowly added. The mixture was stirred for 3 h at −78 °C and for 2 h at −40 °C. Saturated aqueous NH_4Cl (2 mL) was added and the mixture was stirred for a further 10 min at room temperature. The aqueous phase was extracted with diethyl ether, the combined organic phases were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residual oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 70:30 to 50:50) and compound **28** (188 mg, 94% yield, ratio *anti*/*syn* = 54:46) was obtained. The diastereoisomers were then separated by chromatography on silica gel (petroleum ether/ethyl acetate, 70:30, R_f of **28**-*anti* = 0.14 and R_f of **28**-*syn* = 0.06). **28-*anti*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.0 and 0.03 (2 s, 6 H, CH_3, OTBDMS), 0.88 and 1.07 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, TBDMS), 2.64 (m, 1 H, OH), 3.04 (dd, $J_{3/4}$ = 8.10, $J_{4/5}$ = 3.80 Hz, 1 H, 4-H), 3.19 (dd, $J_{4/5}$ = 3.80, $J_{5/6}$ = 6.20 Hz, 1 H, 5-H), 3.35 (dd, $J_{2a/2b}$ = 16.43, $J_{2/3}$ = 3.76 Hz, 1 H, 2-H), 3.43 (dd, $J_{2a/2b}$ = 16.43, $J_{2/3}$ = 8.49 Hz, 1 H, 2-H), 3.62−3.63 (m, 2 H, 7-H), 3.82−3.85 (m, 1 H, 6-H), 4.06−4.14 (m, 1 H, 3-H), 7.33−7.44 (m, C_6H_5), 7.67−7.97 (m, C_6H_5, 2 H, thiazole) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.38 (CH_3, OTBDMS), −5.38 (CH_3, OTBDMS), 18.65, 19.43 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 25.99, 27.05 (*t*Bu, TBDPS,

TBDMS), 44.04 (CH_2, C-2), 58.03 (CH, C-5), 59.09 (CH, C-4), 65.49 (CH, C-3), 65.89 (CH_2, C-7), 70.71 (CH, C-6), 126.51, 127.80, 127.91, 135.82, 136.06, 136.12, 136.20, 144.97 (CH, C_6H_5, thiazole), 133.39, 133.79 (C_q, C_6H_5), 167.17 (C=O) ppm. **28-*syn*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.0 and 0.02 (2 s, 6 H, CH_3, OTBDMS), 0.89 and 1.05 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, TBDMS), 2.98 (dd, $J_{2a/2b}$ = 17.20, $J_{2/3}$ = 2.96 Hz, 1 H, 2-H), 3.02 (dd, $J_{4/5}$ = 4.06, $J_{3/4}$ = 6.77 Hz, 1 H, 4-H), 3.30 (dd, $J_{4/5}$ = 4.06, $J_{5/6}$ = 7.02 Hz, 1 H, 5-H), 3.33 (dd, $J_{2a/2b}$ = 17.20, $J_{2/3}$ = 9.20 Hz, 1 H, 2-H), 3.66−3.75 (m, 2 H, 7-H), 3.82−3.92 (m, 1 H, 6-H, 1 H, 3-H), 7.33−7.44 (m, C_6H_5), 7.67−7.97 (m, C_6H_5, 2 H, thiazole) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.38 (CH_3, OTBDMS), −5.38 (CH_3, OTBDMS), 18.58, 19.47 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 26.12, 27.04 (*t*Bu, TBDPS, TBDMS), 43.23 (CH_2, C-2), 58.16 (CH, C-5), 59.53 (CH, C-4), 65.56 (CH, C-3), 65.96 (CH_2, C-7), 70.72 (CH, C-6), 126.51, 127.80, 127.91, 135.82, 136.06, 136.12, 136.20, 144.97 (CH, C_6H_5, thiazole), 133.39, 133.79 (C_q, C_6H_5), 167.17 (C=O) ppm.

Compound 29: The same experimental procedure as described for the synthesis of compound **30** (see below) was applied, starting from compound **25**-*erythro* (80%). **29-*anti*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.01 and 0.02 (2 s, 6 H, CH_3, OTBDMS), 0.88 and 1.09 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, TBDMS), 1.45 [s, 9 H, $CO_2C(CH_3)_3$], 2.43−2.47 (m, 2 H, 2-H), 2.83 (d, *J* = 3.2 Hz, 1 H, OH), 2.95 (dd, $J_{3/4}$ = 8.24, $J_{4/5}$ = 3.88 Hz, 1 H, 4-H), 3.16 (dd, $J_{4/5}$ = 3.88, $J_{5/6}$ = 6.10 Hz, 1 H, 5-H), 3.57 (d, *J* = 3.96 Hz, 2 H, 7-H), 3.81−3.86 (m, 1 H, 3-H, 1 H, 6-H), 7.38−7.45 (m, C_6H_5), 7.75−7.78 (m, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.45, −5.25 (CH_3, OTBDMS), 18.62, 19.47 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 26.13, 27.12, 28.28 (*t*Bu, TBDPS, TBDMS, CO_2*t*Bu), 40.88 (CH_2, C-2), 57.83 (CH, C-5), 58.89 (CH, C-4), 65.80 (CH_2, C-7), 65.85 (CH, C-3), 70.71 (CH, C-6), 81.21 (C_q, *t*Bu, CO_2*t*Bu), 127.88, 127.97, 130.03, 130.16, 136.10, 136.26 (CH, C_6H_5), 133.33, 134.02 (C_q, C_6H_5), 171.25 (C=O) ppm. MS (DCI, NH_3): *m*/*z* = 601 [M + H^+], 618 [M + NH_4^+]. $C_{33}H_{52}O_6Si_2$ (600.9): calcd. C 65.96, H 8.72; found C 65.71, H 8.81. **29-*syn*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.01 and 0.01 (2 s, 6 H, CH_3, OTBDMS), 0.88 and 1.07 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, TBDMS), 1.45 [s, 9 H, $CO_2C(CH_3)_3$], 2.24−2.25 (m, 2 H, 2-H), 2.90 (dd, $J_{3/4}$ = 7.02, $J_{4/5}$ = 4.27 Hz, 1 H, 4-H), 3.20 (dd, $J_{4/5}$ = 4.27, $J_{5/6}$ = 7.02 Hz, 1 H, 5-H), 3.57−3.81 (m, 2 × 7-H, 1 × 3-H, 1 × 6-H), 7.37−7.46 (m, C_6H_5), 7.69−7.76 (m, C_6H_5) ppm. MS (DCI, NH_3): *m*/*z* = 601 [M + H^+], 618 [M + NH_4^+].

Compound 30: A solution of *n*BuLi (1.6 M in hexane, 238 μL, 0.38 mmol) was added at −78 °C to a solution of diisopropylamine (38 mg, 0.38 mmol) in diethyl ether (1 mL). After the mixture had been stirred for 30 min, *tert*-butyl acetate (44 mg, 0.38 mmol) was added. After 1 h, a solution of aldehyde **25**-*threo* (74 mg, 0.152 mmol) in diethyl ether (2 mL) was slowly added. The mixture was stirred for 1 h at −50 °C and for 1 h at −30 °C. Saturated aqueous NH_4Cl (1 mL) was added and the mixture was stirred for a further 10 min at room temperature. The aqueous phase was extracted with diethyl ether and the combined organic phases were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residual oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 70:30), affording compound **30** (79 mg, 87% yield, ratio *anti*/*syn* = 94:6). The diastereoisomers were separated by chromatography on silica gel (petroleum ether/diethyl ether, 70:30, R_f of **30**-*anti* = 0.52 and R_f of **30**-*syn* = 0.28). **30-*anti*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.03 and 0.01 (2s, 6 H, CH_3, OTBDMS), 0.82 and 1.11 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, TBDMS), 1.45 [s, 9 H, $CO_2C(CH_3)_3$], 2.44 (dd, $J_{2a/2b}$ = 14.89, $J_{2/3}$ = 8.12 Hz, 1 H, 2-H), 2.51 (dd, $J_{2a/2b}$ = 14.89, $J_{2/3}$ = 3.69 Hz, 1 H, 2-H), 2.99 (dd, $J_{3/4}$ = 8.85, $J_{4/5}$ = 4.24 Hz, 1 H, 4-H), 3.11 (dd, $J_{4/5}$ = 4.24, $J_{5/6}$ = 7.93 Hz, 1 H, 5-H), 3.38−3.71 (m, 2 × 7-H, 1 × 3-H, 1 × 6-H), 7.38−7.45 (m, C_6H_5), 7.69−7.72 (m, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.47, −5.34 (CH_3, OTBDMS), 18.83, 19.58 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 26.23, 27.11, 28.27 (*t*Bu, TBDPS, TBDMS, CO_2*t*Bu), 41.18 (CH_2, C-2), 58.82 (CH, C-4), 60.18 (CH, C-5), 65.75 (CH_2, C-7), 67.03, 72.24 (CH, C-3, C-6), 80.94 (C_q, *t*Bu, CO_2*t*Bu), 127.75, 127.86, 130.01, 130.06, 136.12, 136.22 (CH, C_6H_5), 133.30, 133.95 (C_q, C_6H_5), 170.41 (C=O) ppm. **30-*syn*:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.02 and −0.01 (2 s, 6 H, CH_3, OTBDMS), 0.83 and 1.10 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, TBDMS), 1.43 [s, 9 H, $CO_2C(CH_3)_3$], 2.33−2.54 (m, 2 H, 2-H), 3.03 (dd, $J_{3/4}$ = 5.80, $J_{4/5}$ = 4.40 Hz, 1 H, 4-H), 3.17 (dd, $J_{4/5}$ = 4.40, $J_{5/6}$ = 8.54 Hz, 1 H, 5-H), 3.37−3.71 (m, 2 × 7-H, 1 × 3-H, 1 × 6-H), 7.37−7.46 (m, C_6H_5), 7.69−7.76 (m, C_6H_5) ppm.

Bicyclic Compounds 31a and 31b: BF_3−diethyl ether (180 μL, 1.47 mmol) was added dropwise at −78 °C (bath of dry ice and ethanol) to a solution of aldehyde **13** (500 mg, 1.45 mmol) and ethyl 2-(trimethylsilyloxy)-2-propenoate (**6**, 415 mg, 2.20 mmol) in dry dichloromethane (10 mL). The solution was stirred at −78 °C for 3 h and was then allowed to warm to −40 °C and stirred at this temperature for a further 2 h. Saturated aqueous $NaHCO_3$ (8 mL) was added and the mixture was stirred for a further 15 min at room temperature. The aqueous phase was extracted with dichloromethane (10 mL) and ethyl acetate (2 × 15 mL). The combined organic phases were dried with $MgSO_4$ and filtered, and solvents were evaporated. The residual oil was purified by chromatography on a silica gel column (petroleum ether/dichloromethane/ethyl acetate, 4:4.8:1.2, R_f of isomer **31a** = 0.46, R_f of isomer **31b** = 0.37) and bicyclic compound **31a** (152 mg, 32% yield) and bicyclic compound **31b** (48 mg, 13% yield) were obtained. **31a:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.07 (s, 9 H, *t*Bu), 1.31 (t, *J* = 7.15 Hz, 3 H, CH_3, ethyl), 1.88 (dd, $J_{3b/3a}$ = 12.8, $J_{3b/4}$ = 3.4 Hz, 1 H, 3-H), 2.40 (dd, $J_{3a/4}$ = 9.8, $J_{3a/3b}$ = 12.8 Hz, 1 H, 3-H), 3.61 (dd, $J_{6/7}$ = 8.2, $J_{7a/7b}$ = 10.0 Hz, 1 H, 7-H), 3.65 (dd, $J_{7a/6}$ = 5.6, $J_{7a/7b}$ = 10.0 Hz, 1 H, 7-H), 4.27 (q, *J* = 7.15 Hz, 2 H, CO_2Et), 4.60 (m, 1 H, 4-H), 4.71 (d, $J_{5/4}$ = 4.6 Hz, 1 H, 5-H), 4.67 (dd, $J_{6/7a}$ = 5.8, $J_{6/7b}$ = 8.1 Hz, 1 H, 6-H), 4.76 (d, $J_{5/4}$ = 4.7 Hz, 1 H, 5-H), 7.36−7.64 (m, 10 H, CH, TBDPS) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (CH_3, ethyl), 19.2 (C_q, *t*Bu), 26.8 (CH_3, *t*Bu), 43.3 (C-3), 62.3 (CH_2CO_2Et), 63.0 (C-7), 68.5 (C-4), 74.3 (C-6), 80.4 (C-5), 106.1 (C-2), 127.7, 129.8, 135.5 (CH, phenyl), 133.6, 134.1 (C_q, phenyl), 165.7 (C-1) ppm. MS (DCI, NH_3): *m*/*z* = 474 [M + NH_4^+]. $C_{25}H_{32}O_6Si$ (456.2): calcd. C 65.76, H 7.06; found C 66.08, H 6.95. IR (film): $\tilde{\nu}$ = 3506 cm^{-1}, 3072, 3050, 2932, 1752, 1114. **31b:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.05 (s, 9 H, *t*Bu), 1.32 (t, *J* = 7.15 Hz, 3 H, CH_3, ethyl), 1.88 (dd, $J_{3b/3a}$ = 13.5, $J_{3b/4}$ = 1.5 Hz, 1 H, 3-H), 2.56 (dd, $J_{3a/4}$ = 6.5, $J_{3a/3b}$ = 13.5 Hz, 1 H, 3-H), 3.54 (t, $J_{6/7}$ = $J_{7a/7b}$ = 9.5 Hz, 1 H, 7-H), 3.61 (dd, $J_{7a/6}$ = 4.5, $J_{7a/7b}$ = 9.9 Hz, 1 H, 7-H), 3.69 (dd, $J_{6/7a}$ = 4.5, $J_{6/7b}$ = 9.1 Hz, 1 H, 6-H), 4.25 (dd, $J_{4/3a}$ = 6.5, $J_{4/3b}$ = 1.5 Hz, 1 H, 4-H), 4.31 (q, *J* = 7.15 Hz, 2 H, CO_2Et), 4.76 (s, 1 H, 5-H), 7.34−7.66 (m, 10 H, CH, TBDPS) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (CH_3, ethyl), 19.2 (C_q, *t*Bu), 26.8 (CH_3, *t*Bu), 47.3 (C-3), 62.4 (CH_2CO_2Et), 63.1 (C-7), 72.3 (C-4), 75.9 (C-6), 84.3 (C-5), 104.1 (C-2), 127.8, 129.9, 135.5 (CH, phenyl), 133.1, 133.2 (C_q, phenyl), 165.4 (C-1) ppm.

Bicyclic Compounds 32a and 32b. Method A: BF_3−diethyl ether (70 μL, 0.56 mmol) was added dropwise at −78 °C (bath of dry ice and ethanol) to a solution of aldehyde **24**-*erythro* (340 mg,

0.56 mmol) and ethyl 2-(trimethylsilyloxy)-2-propenoate (**6**, 157 mg, 0.84 mmol) in dry dichloromethane (5 mL). The temperature was allowed to warm to −40 °C over 3 h and the mixture was stirred at this temperature for a further 1 h. Saturated aqueous $NaHCO_3$ (2 mL) was added and the mixture was stirred for a further 15 min at room temperature. The aqueous phase was extracted with dichloromethane (10 mL) and ethyl acetate (2 × 15 mL). The combined organic phases were dried with $MgSO_4$ and filtered, and solvents were evaporated. The residual oil was purified by chromatography on a silica gel column (petroleum ether/diethyl ether, 6:4). Starting material aldehyde **24**-*erythro* (160 mg), bicyclic compound **32a** (105 mg) and bicyclic compound **32b** (64 mg) were isolated (41% yield). **Method B:** 78% yield (as described for the synthesis of compounds **33a** and **33b**). **32a:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.02 (s, 9 H, *t*Bu), 1.07 (s, 9 H, *t*Bu), 1.23 (t, J = 7.2 Hz, 3 H, CH_3, ethyl), 1.81 (dd, $J_{3b/3a}$ = 12.7, $J_{3b/4}$ = 3.6 Hz, 1 H, 3-H), 2.38 (dd, $J_{3a/4}$ = 9.9, $J_{3a/3b}$ = 12.6 Hz, 1 H, 3-H), 3.56 (dd, $J_{8b/7}$ = 3.7, $J_{8a/8b}$ = 10.9 Hz, 1 H, 8-H), 3.64 (dd, $J_{8a/7}$ = 3.7, $J_{8a/8b}$ = 10.9 Hz, 1 H, 8-H), 3.94 (td, $J_{7/8a}$ = $J_{7/8b}$ = 3.7, $J_{7/6}$ = 6.1 Hz, 1 H, 7-H), 4.23 (m, 2 H, CH_2, ethyl), 4.49−4.43 (m, 1 H, 4-H), 4.71 (d, $J_{5/4}$ = 4.6 Hz, 1 H, 5-H), 4.77 (d, J = 6.1 Hz, 1 H, 6-H), 7.29−7.73 (m, 20 H, CH, TBDPS) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (CH_3, ethyl), 19.3, 19.5 (C_q, *t*Bu), 26.9, 27.0 (CH_3, *t*Bu), 43.1 (CH_2, C-3), 61.9 (CH_2CO_2Et), 64.9 (CH_2, C-8), 68.5 (CH, C-4), 73.8, 74.4 (CH, C-6 and CH, C-7), 79.8 (CH, C-5), 105.7 (C_q, C-2), 165.7 (C_q, CO_2Et), 127.5, 129.7, 135.7, 135.9, 136.1 (CH, phenyl), 133.6, 134.1 (C_q, phenyl) ppm. $C_{42}H_{52}O_7Si_2$ (725.04): calcd. C 69.58, H 7.23 found C 69.48, H 7.38. $[\alpha]_D^{25}$ = +2.3 (c = 0.6, $CHCl_3$). **32b:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.03 (s, 9 H, *t*Bu), 1.08 (s, 9 H, *t*Bu), 1.29 (t, J = 7.6 Hz, 3 H, CH_3 ethyl), 1.65 (d, $J_{3b/3a}$ = 13.5 Hz, 1 H, 3-Hb), 2.50 (dd, $J_{3a/4}$ = 6.5 Hz and $J_{3a/3b}$ = 13.5 Hz, 1 H, 3-Ha), 3.50 (dd, $J_{8b/7}$ = 2.8 Hz and $J_{8b/8a}$ = 10.7 Hz, 1 H, 8-Hb), 3.59 (dd, $J_{8a/7}$ = 3.3 Hz and $J_{8a/8b}$ = 10.7 Hz, 1 H, 8-Ha), 3.76 (d, $J_{6/7}$ = 5.9 Hz, 1 H, 6-H), 3.81 (ddd, $J_{7/8a}$ = 3.3, $J_{7/8b}$ = 2.8, $J_{7/6}$ = 5.9 Hz, 1 H, 7-H), 4.06 (d, $J_{4/3a}$ = 6.4 Hz, 1 H, 4-H), 4.27 (q, J = 7.6 Hz, 2 H, CH_2, ethyl), 4.64 (s, 1 H, 5-H), 7.25−7.69 (m, 20 H, CH, TBDPS) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (CH_3, ethyl), 19.5, 19.3 (C_q, *t*Bu), 26.9, 27.0 (CH_3, *t*Bu), 47.0 (CH_2, C-3), 62.0 (CH_2CO_2Et), 64.6 (CH_2, C-8), 72.0 (CH, C-4), 73.4, 76.1 (CH, C-6 and CH, C-7), 83.6 (CH, C-5), 103.9 (C_q, C-2), 127.6, 129.6, 135.6, 135.8, 136.0 (CH, phenyl), 133.2, 133.9 (C_q, phenyl), 165.5 (C_q, CO_2Et) ppm. $C_{42}H_{52}O_7Si_2$ (725.04): calcd. C 69.58, H 7.23; found C 69.13, H 6.86. $[\alpha]_D^{25}$ = +5.6 (c = 0.7, $CHCl_3$).

Diastereoisomers of Bicyclic Compounds 32a and 32b. Method B: As described for the synthesis of compounds **33a** and **33b**, starting from aldehyde **24**-*threo* (40 mg, 0.06 mmol), 23 mg of diastereoisomers of **32a** and **32b** were obtained (50% yield). **Diastereoisomer of 32a:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.01 (s, 9 H, *t*Bu), 1.08 (s, 9 H, *t*Bu), 1.21 (t, J = 7.2 Hz, 3 H, CH_3, ethyl), 1.81 (dd, $J_{3b/3a}$ = 12.7, $J_{3b/4}$ = 3.5 Hz, 1 H, 3-H), 2.33 (dd, $J_{3a/4}$ = 9.9, $J_{3a/3b}$ = 12.7 Hz, 1 H, 3-H), 3.65 (dd, $J_{8b/7}$ = 5.1, $J_{8a/8b}$ = 11.0 Hz, 1 H, 8-H), 3.75 (dd, $J_{8a/7}$ = 4.1, $J_{8a/8b}$ = 11.0 Hz, 1 H, 8-H), 3.96−4.00 (m, 1 H, 7-H), 4.16−4.20 (m, 2 H, CH_2, ethyl), 4.36−4.42 (m, 1 H, 4-H), 4.58 (d, $J_{5/4}$ = 4.7 Hz, 1 H, 5-H), 4.73 (d, J = 6.5 Hz, 1 H, 6-H), 7.30−7.74 (m, 20 H, CH, TBDPS) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (CH_3, ethyl), 19.3, 19.5 (C_q, *t*Bu), 26.9, 27.0 (CH_3, *t*Bu), 43.4 (CH_2, C-3), 62.0 (CH_2CO_2Et), 65.4 (CH_2, C-8), 68.8 (CH, C-4), 73.9, 75.7 (CH, C-6 and CH, C-7), 79.6 (CH, C-5), 106.1 (C_q, C-2), 165.7 (C_q, CO_2Et), 127.5, 129.7, 135.7, 135.9, 136.1 (CH, phenyl), 133.6, 134.1 (C_q, phenyl) ppm. MS: (DCI, NH_3): m/z = 742 [M + NH_4^+]. **Diastereoisomer of 32b:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.03 (s, 9 H, *t*Bu), 1.04 (s, 9 H, *t*Bu), 1.09 (t, J = 7.6 Hz, 3 H, CH_3, ethyl), 1.65 (d, $J_{3b/3a}$ = 13.5 Hz, 1 H, 3-Hb), 2.46 (dd, $J_{3a/4}$ = 6.5 Hz and $J_{3a/3b}$ = 13.5 Hz, 1 H, 3-Ha), 3.56 (d, $J_{6/7}$ = 6.4 Hz, 1 H, 6-H), 3.63 (dd, $J_{8b/7}$ = 5.16 Hz and $J_{8b/8a}$ = 11.1 Hz, 1 H, 8-Hb), 3.68 (dd, $J_{8a/7}$ = 3.94 Hz and $J_{8a/8b}$ = 11.1 Hz, 1 H, 8-Ha), 3.83−3.90 (m, 1 H, 4-H), 3.91−3.93 (m, 1 H, 7-H), 4.27 (q, J = 7.6 Hz, 2 H, CH_2, ethyl), 4.62 (s, 1 H, 5-H), 7.26−7.70 (m, 20 H, CH, TBDPS) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (CH_3, ethyl), 19.5, 19.3 (C_q, *t*Bu), 26.9, 27.0 (CH_3, *t*Bu), 47.1 (CH_2, C-3), 62.0 (CH_2CO_2Et), 65.1 (CH_2, C-8), 72.2 (CH, C-4), 73.8, 77.2 (CH, C-6 and CH, C-7), 83.5 (CH, C-5), 104.3 (C_q, C-2), 127.6, 129.6, 135.6, 135.8, 136.0 (CH, phenyl), 133.2, 133.9 (C_q, phenyl), 165.4 (C_q, CO_2Et) ppm. MS (DCI, NH_3): m/z = 725 [M + H^+], 742 [M + NH_4^+].

Bicyclic Compounds 33a and 33b. Method B: BF_3−diethyl ether (390 μL, 3.10 mmol) was added, dropwise at −45 °C (bath of dry ice and acetonitrile), to a solution of aldehyde **25**-*erythro* (229 mg, 0.47 mmol) and ethyl 2-(trimethylsilyloxy)-2-propenoate (**6**) (414 mg, 2.07 mmol) in dry dichloromethane (15 mL). After the mixture had been stirred at −45 °C for 6 h, saturated aqueous $NaHCO_3$ (5 mL) was added and the mixture was stirred for a further 15 min at room temperature. The aqueous phase was extracted with dichloromethane (10 mL) and ethyl acetate (2 × 15 mL). The combined organic phases were dried with $MgSO_4$ and filtered, and solvents were evaporated. The residual oil was purified by chromatography on a silica gel column (eluent petroleum ether/diethyl ether, 6:4). Bicyclic compound **33** (217 mg, 77% yield) and deprotected bicyclic compound **31** (23 mg, 10% yield) were isolated. The diastereoisomers **33a** and **33b** (*dr* 85:15) were separated by HPLC {silica, eluent M6 [M6 = hexane/M0 (60:40); M0 = dichloromethane/ethylacetate (80:20)], R_f of major isomer = 0.28 and R_f of minor isomer = 0.16}. **33a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.06 (s, 6 H, CH_3, OTBDMS), 0.85 and 1.07 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, OTBDMS), 1.31 (t, J = 7.14 Hz, 3 H, $CO_2CH_2CH_3$), 1.75−1.80 (m, 1 H, OH), 1.82 (dd, $J_{3a/3b}$ = 12.73, $J_{3/4}$ = 3.57 Hz, 1 H, 3-H), 2.38 (dd, $J_{3a/3b}$ = 12.73, $J_{3/4}$ = 9.85 Hz, 1 H, 3-H), 3.53−3.55 (m, 2 H, 8-H), 3.82−3.85 (m, 1 H, 7-H), 4.28 (q, J = 7.14 Hz, 2 H, $CO_2CH_2CH_3$), 4.48−4.57 (m, 1 H, 4-H), 4.65 (d, $J_{6/7}$ = 6.77 Hz, 1 H, 6-H), 4.75 (d, $J_{4/5}$ = 4.67 Hz, 1 H, 5-H), 7.33−7.43 (m, C_6H_5), 7.69−7.76 (m, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.38 (CH_3, OTBDMS), −5.38 (CH_3, OTBDMS), 14.22 ($CO_2CH_2CH_3$), 18.56, 19.72 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 25.98, 26.12 (*t*Bu, TBDPS, TBDMS), 43.33 (CH_2, C-3), 62.15 ($CO_2CH_2CH_3$), 64.04 (CH_2, C-8), 68.81 (CH, C-4), 74.18 (CH, C-7), 74.64 (CH, C-6), 80.21 (CH, C-5), 105.98 (C_q, C-2), 127.70, 129.77, 136.13 (CH, C_6H_5), 134.11, 134.55 (C_q, C_6H_5), 165.96 (C=O, $CO_2CH_2CH_3$) ppm. MS (DCI, NH_3): m/z = 618 [M + NH_4^+]. $C_{32}H_{48}O_7Si_2$ (600.3): calcd. C 63.96, H 8.05; found C 63.74, H 7.96. IR (film, cm^{-1}): $\tilde{\nu}$ = 3510, 3072, 3050, 2955, 2931, 2894, 2857, 1751, 1590, 1473, 1428, 1379, 1361, 1347, 1252, 1204, 1111, 1029, 975, 917, 837. $[\alpha]_D^{25}$ = +6.43 (c = 2.49, $CHCl_3$). **33b:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = −0.10 and −0.08 (s, 3 H each singlet, CH_3, TBDMS), 0.84 and 1.08 (s, 9 H each singlet, *t*Bu, OTBDPS, *t*Bu, TBDMS), 1.33 (t, J = 7.12 Hz, 3 H, $CO_2CH_2CH_3$), 1.86 (dt, $J_{3a/3b}$ = 13.43, $J_{3/5}$ = 1.12 Hz,1 H, 3-H), 2.04 (d, $J_{OH/4}$ = 9.16 Hz, 1 H, OH), 2.50 (dd, $J_{3a/3b}$ = 13.43, $J_{3/4}$ = 6.41 Hz, 1 H, 3-H), 3.46 (d, J = 3.68 Hz, 2 H, 8-H), 3.71 (d, J = 6.08 Hz, 1 H, 6-H), 3.74−3.76 (m, 1 H, 7-H), 4.10−4.20 (m, 1 H, 4-H), 4.31 (q, J = 7.12 Hz, 2 H, $CO_2CH_2CH_3$), 4.75 (d, $J_{5/3}$ = 1.12 Hz, 1 H, 5-H), 7.38−7.44 (m, C_6H_5), 7.70−7.75 (m, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.51 (CH_3, OTBDMS), −5.39 (CH_3, OTBDMS), 14.24 ($CO_2CH_2CH_3$), 18.56, 19.67 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 26.07, 27.15 (*t*Bu, TBDPS, TBDMS), 47.34 (CH_2, C-3), 62.31 ($CO_2CH_2CH_3$), 63.77 (CH_2, C-8), 72.27 (CH, C-4),

73.74 (CH, C-7), 76.31 (CH, C-6), 83.98 (CH, C-5), 104.05 (C_q, C-2), 127.75, 127.87, 129.84, 129.96, 136.07, 136.19 (CH, C_6H_5), 133.72, 134.48 (C_q, C_6H_5), 165.80 (C=O, $CO_2CH_2CH_3$) ppm. MS (DCI, NH_3): m/z = 601 [M + H^+], 618 [M + NH_4^+]. IR (film, cm^{-1}): $\tilde{\nu}$ = 3510, 3072, 3050, 2955, 2931, 2894, 2857, 1751, 1590, 1473, 1428, 1379, 1361, 1347, 1252, 1204, 1111, 1029, 975, 917, 837. $[\alpha]_D^{25}$ = +8.65 (c = 1.96, $CHCl_3$). **34a:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (s, 9 H, *t*Bu, OTBDPS), 1.28 (t, J = 7.00 Hz, 3 H, $CO_2CH_2CH_3$), 1.80 (dd, J = 12.82, J = 3.05 Hz, 1 H, 3-H), 2.30−2.50 (m, 1 × 3-H, 1 H, OH), 3.50−3.70 (m, 2 H, 8-H), 3.70−3.90 (m, 1 H, 7-H), 4.23 (q, J = 7.00 Hz, 2 H, $CO_2CH_2CH_3$), 4.35−4.50 (m, 1 ×4-H, 1 × 5-H), 4.65 (d, J = 7.63 Hz, 1 H, 6-H), 7.36−7.70 (m, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.94 ($CO_2CH_2CH_3$), 19.41 (C_q, *t*Bu, TBDPS), 27.00 (*t*Bu, TBDPS), 42.81 (CH_2, C-3), 62.35 ($CO_2CH_2CH_3$), 64.03 (CH_2, C8), 68.34 (CH-4), 72.75 (CH), 76.19 (CH), 80.87 (CH, C5), 105.98 (Cq, C2), 127.87, 127.94, 135.71, 135.90 (CH, C_6H_5), 133.35, 133.44 (C_q, C_6H_5), 165.51 (C=O, $CO_2CH_2CH_3$) ppm. MS (DCI, NH_3): m/z = 504 [M + NH_4^+].

Compound 37: Et_3N (0.50 mL) and acetic anhydride (0.25 mL) were added at room temperature to a solution of alcohol **33a** (56 mg, 0.093 mmol) and DMAP (25 mg, 0.205 mmol) in dry CH_2Cl_2 (3 mL). The solution was stirred for 5 h. The organic phase was washed with saturated aqueous $NaHCO_3$ and then brine, dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 6:4, R_f = 0.60) and the desired product (56 mg, 94% yield) was obtained. ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.13 (s, 3 H, CH_3, OTBDMS), 0.82 (s, 9 H, *t*Bu, OTBDMS), 1.04 (s, 9 H, *t*Bu, OTBDPS), 1.29 (t, J = 7.33 Hz, 3 H, $CO_2CH_2CH_3$), 1.95 (dd, J = 12.82, J = 3.06 Hz, 1 H, 3-H), 2.50 (dd, J = 12.82, J = 9.46 Hz, 1 H, 3-H), 3.41−3.43 (m, 2 H, 8-H), 3.71−3.77 (m, 1 H, 7-H), 4.26 (q, J = 7.33 Hz, 2 H, $CO_2CH_2CH_3$), 4.50 (d, J = 7.33 Hz, 1 H, 6-H), 5.05−5.12 (m, 1 H, 5-H, 1 H, 4-H), 7.32−7.72 (m, 10 H, C_6H_5) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = −5.73 (CH_3, OTBDMS), −5.58 (CH_3, OTBDMS), 14.01 ($CO_2CH_2CH_3$), 18.27, 19.44 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 20.63 (CH_3, OAc), 25.84, 26.91 (*t*Bu, TBDPS, TBDMS), 40.94 (CH_2, C-3), 62.09 ($CO_2CH_2CH_3$), 63.06 (CH_2, C-8), 70.14 (CH, C-4), 73.38 (CH, C-7), 75.03 (CH, C-6), 78.15 (CH, C-5), 105.23 (C_q, C-2), 127.49, 127.64, 129.71 135.87, 135.97 (CH, C_6H_5), 133.41, 134.38 (C_q, C_6H_5), 165.96 (C=O, $CO_2CH_2CH_3$), 170.42 (C=O, OAc) ppm. MS (DCI, NH_3): m/z = 660 [M + NH_4^+]. IR (film, cm^{-1}): $\tilde{\nu}$ = 3072, 2995, 2931, 2857, 1748, 1590, 1473, 1428, 1376, 1235, 1206, 1111, 1039, 836, 779, 741, 704.

Compound 38: BF_3−Et_2O (22 mg, 0.155 mmol) was slowly added at −30 °C to a solution of silyl ether **37** (50 mg, 0.078 mmol) in dry CH_2Cl_2 (4 mL). The solution was allowed to warm to −3 °C over 1 h. Saturated aqueous $NaHCO_3$ was added, and the aqueous phase was extracted with ethyl acetate. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 6:4 R_f = 0.14) and the desired product (43 mg, quantitative) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (s, 9 H, *t*Bu, OTBDPS), 1.28 (t, J = 7.14 Hz, 3 H, $CO_2CH_2CH_3$), 1.93 (dd, J = 3.36, J = 13.12 Hz, 1 H, 3-H), 2.12 (s, 3 H, $OCOCH_3$), 2.53 (dd, J = 10.07, J = 13.12 Hz, 1 H, 3-H), 3.58−3.65 (m, 2 H, 8-H), 3.73 (ddd, $J_{7/6}$ = 8.19, $J_{7/8}$ = 8.00, $J_{7/8}$ = 8.06 Hz, 1 H, 7-H), 4.25 (q, J = 7.14 Hz, 2 H, $CO_2CH_2CH_3$), 4.43 (d, $J_{6/7}$ = 8.19 Hz, 1 H, 6-H), 4.72 (d, $J_{5/4}$ = 4.74 Hz, 1 H, 5-H), 5.05 (ddd, $J_{5/4}$ = 4.74, J = 4.67, J = 10.03 Hz, 1 H, 4-H), 7.33−7.43 (m, C_6H_5), 7.69−7.76 (m, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.12 ($CO_2CH_2CH_3$), 19.54 (C_q, TBDPS), 20.90 (CH_3, OAc), 27.17 (*t*Bu, OTBDPS), 40.69 (CH_2, C-3), 62.62 ($CO_2CH_2CH_3$), 63.75 (CH_2, C-8), 70.10 (CH, C-4), 72.82 (CH, C-7), 76.98 (CH, C-6), 79.41 (CH, C-5), 105.72 (C_q, C-2), 128.11, 128.13, 135.85, 136.02 (CH, C_6H_5), 133.22, 133.69 (C_q, C_6H_5), 164.86 (C=O, $OCOCH_3$), 170.53 (C=O, $CO_2CH_2CH_3$) ppm. MS (DCI, NH_3): m/z = 546 [M + NH_4^+]. IR (film, cm^{-1}): $\tilde{\nu}$ = 3519, 3066, 2928, 2856, 1747, 1586, 1463, 1428, 1377, 1236, 1204, 1112, 1068, 971, 944, 822.

Compound 39: Phosphoramidite (120 mg, 0.348 mmol) was slowly added at room temperature to a solution of alcohol **38** (46 mg, 0.087 mmol) and tetrazole (48 mg, 0.696 mmol) in dry CH_2Cl_2 (5 mL). After 65 min, a solution of *m*CPBA (180 mg, 0.696 mmol) in dry CH_2Cl_2 (5 mL) was added at −10 °C. The mixture was stirred for a further 60 min at 0 °C. CH_2Cl_2 (10 mL) was added and the organic phase was washed with aqueous Na_2SO_3 (10%), saturated aqueous $NaHCO_3$, and brine, dried with $MgSO_4$, and filtered, and the solvent was evaporated. The residual oil was purified by chromatography on silica gel (petroleum ether/CH_2Cl_2/ethyl acetate, 5:4:1, R_f = 0.09) and the desired product (49 mg, 72% yield) was obtained. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (s, 9 H, *t*Bu, OTBDPS), 1.21 (t, J = 7.33 Hz, 3 H, $CO_2CH_2CH_3$), 1.89 (dd, J = 3.66, J = 13.13 Hz, 1 H, 3-H), 2.09 (s, 3 H, $OCOCH_3$), 2.46 (dd, J = 10.07, J = 13.13 Hz, 1 H, 3-H), 3.72−3.82 (m, 1 H, 7-H), 3.93−4.13 (m, 2 H, 8-H), 4.17 (q, J = 7.33 Hz, 2 H, $CO_2CH_2CH_3$), 4.47 (d, $J_{6/7}$ = 8.24 Hz, 1 H, 6-H), 4.80 (d, $J_{5/4}$ = 4.88 Hz, 1 H, 5-H), 4.82−4.98 (m,4 H, $OCH_2C_6H_5$), 5.01−5.07 (m, 1 H, 4-H), 7.31−7.69 (m, 20 H, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.96 ($CO_2CH_2CH_3$), 19.42 (C_q, TBDPS), 20.80 (CH_3, OAc), 26.92 (*t*Bu, OTBDPS), 40.54 (CH_2, C-3), 62.27 ($CO_2CH_2CH_3$), 67.58 (d, J = 5.89 Hz, CH_2, C-8), 68.95 (d, J = 5.23 Hz, CH_2, OBn), 69.85 (CH, C-4), 71.37 (d, J = 9.16 Hz, CH, C-7), 74.70 (CH, C-6), 78.69 (CH, C-5), 105.64 (C_q, C-2), 127.80, 127.85, 128.91, 128.43, 128.55, 135.95, 136.62 (CH, C_6H_5), 132.80, 133.09 (C_q, C_6H_5), 164.86 (C=O, $OCOCH_3$), 170.50 (C=O, $CO_2CH_2CH_3$) ppm. MS (DCI, NH_3): m/z = 806 [M + NH_4^+].

Compound 40: TBDPSCl (34 mg, 0.124 mmol) was added at room temperature to a solution of alcohol **33a** (50 mg, 0.083 mmol) and imidazole (17 mg, 0.25 mmol) in dry DMF (0.33 mL). The solution was heated at 70 °C for 21 h. Ethyl acetate (10 mL) was added, and the organic phase was washed with water (5 mL), dried with $MgSO_4$, filtered, and concentrated. The oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 9:1, R_f = 0.37), affording the protected product (49 mg, 71% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = −0.12 (s, 3 H, CH_3, OTBDMS), −0.09 (s, 3 H, CH_3, OTBDMS), 0.83 (s, 9 H, *t*Bu, OTBDMS), 1.08, 1.10 (s, 9 H, *t*Bu, OTBDPS), 1.25 (t, J = 7.33 Hz, 3 H, $CO_2CH_2CH_3$), 1.83 (dd, J = 3.35, J = 12.52 Hz, 1 H, 3-H), 2.02 (dd, J = 9.46, J = 12.52 Hz, 1 H, 3-H), 3.43 (dd, J = 3.66, J = 10.99 Hz, 1 H, 8-H), 3.54 (dd, J = 3.05, J = 10.99 Hz, 1 H, 8-H), 3.70−3.79 (m, 1 H, 7-H), 4.19 (q, J = 7.33 Hz, 2 H, $CO_2CH_2CH_3$), 4.42−4.49 (m, 1 H, 4-H), 4.77 (d, J = 4.88 Hz, 1 H, 5-H), 4.99 (d, J = 7.63 Hz, 1 H, 6-H), 7.32−7.79 (m, C_6H_5) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.63, −5.57 (CH_3, OTBDMS), 13.96 ($CO_2CH_2CH_3$), 18.38, 19.15, 19.58 (C_q, *t*Bu, TBDPS, *t*Bu, TBDMS), 25.97, 26.86, 27.05 (*t*Bu, TBDPS, TBDMS), 43.40 (CH_2, C-3), 61.79 ($CO_2CH_2CH_3$), 62.69 (CH_2, C-8), 69.92 (CH, C-4), 73.70 (CH, C-7), 74.20 (CH, C-6), 79.97 (CH, C-5), 105.97 (C_q, C-2), 127.41, 127.80, 127.85, 129.46, 129.64, 130.14, 135.60, 135.65, 136.06 (CH, C_6H_5), 132.98, 133.34, 133.67, 134.54 (C_q, C_6H_5), 170.53 (C=O, $CO_2CH_2CH_3$) ppm. MS(DCI, NH_3): m/z = 856 [M + NH_4^+]. IR (film, cm^{-1}): $\tilde{\nu}$ = 3072, 3050, 2957, 2893, 2858, 1764, 1590, 1472, 1428, 1391,

1362, 1291, 1205, 1133, 1108, 1043, 1006, 978, 955, 890, 836, 778, 740, 702.

Compound 41: BF_3-Et_2O (24 mg, 0.171 mmol) was added at −20 °C to a solution of silyl ether **40** (72 mg, 0.086 mmol) in dry CH_2Cl_2 (2 mL). The solution was stirred for 50 min at −20 to −5 °C. Dichloromethane (10 mL) was added, and the organic phase was washed with saturated aqueous $NaHCO_3$, dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/diethyl ether, 6:4) to give the desired product (58 mg, 93% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.09 (s, 9 H, *t*Bu, OTBDPS), 1.10 (s, 9 H, *t*Bu, OTBDPS), 1.26 (t, *J* = 7.02 Hz, 3 H, $CO_2CH_2CH_3$), 1.82 (dd, *J* = 3.36, *J* = 12.51 Hz, 1 H, 3-H), 2.05 (dd, *J* = 9.46, *J* = 12.51 Hz, 1 H, 3-H), 2.18 (dd, *J* = 4.88, *J* = 8.55 Hz, 1 H, OH), 3.57−3.63 (m, 2 H, 8-H), 3.75−3.82 (m, 1 H, 7-H), 4.21 (q, *J* = 7.02 Hz, 2 H, $CO_2CH_2CH_3$), 4.38−4.46 (m, 1 H, 4-H), 4.54 (d, *J* = 4.58 Hz, 1 H, 5-H), 4.91 (d, *J* = 7.32 Hz, 1 H, 6-H), 7.31−7.72 (m, 20 H, C_6H_5) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.92 ($CO_2CH_2CH_3$), 19.14, 19.45 (C_q, *t*Bu,TBDPS), 26.86, 27.07 (*t*Bu, TBDPS), 42.99 (CH_2, C-3), 62.22 ($CO_2CH_2CH_3$), 63.83 (CH_2, C-8), 69.74 (CH, C-4), 72.84 (CH, C-7), 76.86 (CH, C-6), 80.69 (CH, C-5), 106.13 (C_q, C-2), 127.88, 130.05, 135.53, 135.62, 135.66, 135.83 (CH, C_6H_5), 132.83, 133.08, 133.84 (C_q, C_6H_5), 165.43 (C=O, $CO_2CH_2CH_3$) ppm. MS (DCI, NH_3): *m*/*z* = 742 [M + NH_4^+]. IR (film, cm^{-1}): ṽ = 3532, 3062, 2931, 2858, 1756, 1660, 1587, 1472, 1428, 1376, 1262, 1189, 1111, 1074, 1050, 968, 907, 823, 740, 703.

Compound 42: A solution of phosphoramidite (105 mg, 0.30 mmol) in dry CH_2Cl_2 (2 mL) was added at room temperature to a solution of alcohol **41** (55 mg, 0.076 mmol) and tetrazole (43 mg, 0.60 mmol) in dry CH_2Cl_2 (1 mL). After 1 h and 30 min, the reaction mixture was cooled to −10 °C and a solution of *m*CPBA (150 mg, 0.60 mmol) in dry CH_2Cl_2 (2 mL) was added. The mixture was stirred for a further 65 min at 0 °C. CH_2Cl_2 (10 mL) was added, and the organic phase was washed with aqueous Na_2SO_3 (10%), saturated aqueous $NaHCO_3$, and brine. The organic phase was dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/CH_2Cl_2/ethyl acetate, 5:4:1, R_f = 0.35) affording the desired compound (66 mg, 88% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.06 (s, 9 H, *t*Bu, OTBDPS), 1.10 (s, 9 H, *t*Bu, OTBDPS), 1.20 (t, *J* = 7.12 Hz, 3 H, $CO_2CH_2CH_3$), 1.78 (dd, *J* = 3.36, *J* = 12.51 Hz, 1 H, 3-H), 1.99 (dd, *J* = 9.46, *J* = 12.51 Hz, 1 H, 3-H), 3.78−3.90 (m, 1 H, 7-H), 3.93−4.05 (m, 2 H, 8-H), 4.11 (q, *J* = 7.12 Hz, 2 H, $CO_2CH_2CH_3$), 4.37−4.45 (m, 1 H, 4-H), 4.61 (d, *J* = 4.58 Hz, 1 H, 5-H), 4.80−5.03 [m, 1 H, 6-H, 4 H, $P(O)(OCH_2C_6H_5)_2$], 7.21−7.74 (m, 30 H, C_6H_5) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.90 ($CO_2CH_2CH_3$), 19.14, 19.54 (C_q, *t*Bu, TBDPS), 26.82, 27.02 (*t*Bu, TBDPS), 43.02 (CH_2, C-3), 61.98 ($CO_2CH_2CH_3$), 67.45 (d, *J* = 5.31 Hz, CH_2, C-8), 68.82, 68.91 [2 d, *J* = 5.32 Hz, CH_2, $P(O)(OCH_2C_6H_5)$], 69.69 (CH, C4), 71.72 (d, *J* = 9.01 Hz, CH, C-7), 74.23 (CH, C-6), 80.04 (CH, C-5), 106.25 (C_q, C-2), 127.70 127.77, 128.24, 128.44, 129.82, 129.95, 130.02, 135.53, 135.58, 135.93, (CH, C_6H_5), 132.80, 132.96, 133.10, 133.34 (C_q, C_6H_5), 165.36 (C=O, $CO_2CH_2CH_3$) ppm. ^{31}P NMR ($CDCl_3$, 81 MHz): δ = −1.04 ppm. MS (DCI, NH_3): *m*/*z* = 985 [M + H^+], 1002 [M + NH_4^+]. IR (film, cm^{-1}): ṽ = 3060, 2931, 2858, 1752, 1589, 1456, 1428, 1379, 1266, 1207, 1106, 1040, 1021, 886, 823, 740.

Compound 43: A solution of TBAF (1 M, 60 μL, 0.060 mmol) was added at room temperature to a solution of silyl ether **42** (40 mg, 0.040 mmol) in dry THF (0.3 mL). The solution was stirred for 1 h. Diethyl ether (2 mL) was added, and the organic phase was washed with brine, dried with $MgSO_4$, filtered, and concentrated. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 50:50 to 0:100), and the diol (11 mg, 50% yield) was obtained. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.12 Hz, 3 H, $COCH_2CH_3$), 1.87 (dd, *J* = 12.86, *J* = 3.36 Hz, 1 H, 3-H), 2.40 (dd, *J* = 12.86, *J* = 9.77 Hz, 1 H, 3-H), 3.70−3.80 (m, 1 H, 7-H), 4.04−4.18 (m, 2 H, 8-H, 2 H, $CO_2CH_2CH_3$), 4.50−4.60 (m, 1 H, 4-H), 4.54 (d, *J* = 7.63 Hz, 1 H, 6-H), 4.84 (d, *J* = 4.58 Hz, 1 H, 5-H), 5.01−5.06 (m, 4 H, 2 × $OCH_2C_6H_5$), 7.34 (br. s, 10 H, C_6H_5) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.05 ($CO_2CH_2CH_3$), 42.56 (CH_2, C-3), 62.30 ($CO_2CH_2CH_3$), 68.14 (CH), 68.65 (d, *J* = 5.31 Hz, CH_2, C-8), 69.82 [2 d, *J* = 5.32 Hz, CH_2, $P(O)(CH_2C_6H_5)$], 73.50 (CH), 80.28 (CH), 106.33 (C_q, C-2), 128.11, 128.71, 128.78 (CH, C_6H_5), 165.36 (C=O, $CO_2CH_2CH_3$) ppm. ^{31}P NMR (81 MHz, $CDCl_3$): δ = 0.35 ppm.

Compound 45: A solution of $SnCl_4$ in CH_2Cl_2 (1 M, 61 μL, 0.061 mmol) was added at room temperature to a solution of bicyclic compound **33a** (29 mg, 0.061 mmol) in methanol (1 mL). The solution was stirred for 49 h at room temperature. The mixture was cooled at 0 °C (ice bath), and ethyl acetate (5 mL) and aqueous $NaHCO_3$ (10%, 1 mL) were added. The organic phase was washed with brine, dried with $MgSO_4$, and filtered, and the solvents were evaporated. The residual oil was purified by chromatography on silica gel [petroleum ether/ethyl acetate, 1:1, R_f = 0.19 (product) and R_f = 0.33 (starting material)], and starting material (9.8 mg) and an inseparable mixture of α- and β-methyl furanosidic compounds **45** (19.2 mg) were obtained (62% yield, 94% yield based on recovered starting material). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (s, 9 H of α-methyl isomer and 9 H of β-methyl isomer, *t*Bu, OTBDPS), 2.36 (dd, $J_{3a/3b}$ = 14.03, $J_{3/4}$ = 4.00 Hz, 1 H, 3-H of α-methyl isomer and 1 H, 3-H of β-methyl isomer), 2.44 (dd, $J_{3a/3b}$ = 14.03, $J_{3/4}$ = 5.96 Hz, 1 H, 3-H of α-methyl isomer and 1 H, 3-H of β-methyl isomer), 3.22 and 3.39 (2 s, 3 H, OCH_3 of α-methyl isomer and 3 H, OCH_3 of β-methyl isomer), 3.59−3.78 (m, 2 H, 8-H of α-methyl isomer and 2 H, 8-H of β-methyl isomer), 3.79 and 3.83 (2 s, 3 H, CO_2CH_3 of α-methyl isomer and 3 H, CO_2CH_3 of β-methyl isomer), 3.91−3.98 (m, 1 H, 7-H of α-methyl isomer and 1 H, 7-H of β-methyl isomer), 4.09−4.17 (m, 1 H, 6-H of α-methyl isomer and 1 H, 6-H of β-methyl isomer), 4.40 (dd, *J* = 2.58, *J* = 4.19 Hz, 1 H, 5-H of one isomer), 4.42−4.49 (m, 1 H, 4-H of one isomer), 4.52 (dd, *J* = 1.29, *J* = 5.29 Hz, 1 H, 5-H of one isomer), 4.54−4.60 (m, 1 H, 4-H of one isomer), 7.38−7.77 (m, C_6H_5 of α- and β-methyl isomers) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.40 (C_q, *t*Bu, TBDPS), 27.05 (*t*Bu, TBDPS), 45.37 and 46.76 (CH_2, C-3 of α- and β-methyl isomers), 51.97, 52.69, 53.13 (CO_2CH_3 of α- and β-methyl isomers and OCH_3 of α- and β-methyl isomers), 63.64 and 64.11 (CH_2, C-8 of α- and β-methyl isomers), 72.05 and 72.65 (CH, C-6 of α- and β-methyl isomers), 73.18 and 73.37 (CH, C-4 of α- and β-methyl isomers), 73.86 and 74.05 (CH, C7 of α- and β-methyl isomers), 80.52 and 83.45 (CH, C-5 of α- and β-methyl isomers), 105.69 (C_q, C-2 of α- and β-methyl isomers), 127.88, 130.05, 135.87 (CH, C_6H_5), 133.72, 135.69 (C_q, C_6H_5), 171.13 (C=O, CO_2CH_3) ppm. MS (DCI, NH_3): *m*/*z* = 505 [M + H^+], 522 [M + NH_4^+]. IR (film, cm^{-1}): ṽ = 3510, 3072, 3050, 2955, 2931, 2894, 2857, 1751, 1590, 1473, 1428, 1379, 1361, 1347, 1252, 1204, 1111, 1029, 975, 917, 837.

Compound 51: Triethyl phosphite (17 μL, 0.098 mmol) was added at 0 °C to a solution of α- and β-methyl furanoside compound **45** (40 mg, 0.079 mmol) and CBr_4 (31 mg, 0.09 mmol) in pyridine (0.5 mL). The ice bath was removed and the mixture was stirred for 21 h. Diethyl ether (5 mL) was added, and the organic phase was washed with saturated aqueous NH_4Cl (2 mL) and then with

brine (2 mL), dried with $MgSO_4$, filtered, and concentrated. The residual oil was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 1:1), affording compound **51** (40 mg, 80% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.06 (s, 9 H of α-methyl isomer and 9 H of β-methyl isomer, *t*Bu, OTBDPS), 1.32 (t, *J* = 7.02 Hz, OCH_2CH_3), 2.36 (dd, $J_{3a/3b}$ = 14.03, $J_{3/4}$ = 4.00 Hz, 1 H, 3-H of α-methyl isomer and 1 H, 3-H of β-methyl isomer), 2.44 (dd, $J_{3a/3b}$ = 14.03, $J_{3/4}$ = 5.96 Hz, 1 H, 3-H of α-methyl isomer and 1 H, 3-H of β-methyl isomer), 3.18 and 3.35 (2s, 3 H, OCH_3 of α-methyl isomer and 3 H, OCH_3 of β-methyl isomer), 3.58 (dd, *J* = 4.28, *J* = 12.21 Hz, 1 H, 8-H of one isomer), 3.65 (dd, *J* = 4.27, *J* = 12.21 Hz, 1 H, 8-H of one isomer), 3.75 and 3.79 (2 s, 3 H, CO_2CH_3 of α-methyl isomer and 3 H, CO_2CH_3 of β-methyl isomer), 3.91−3.93 (m, 1 H, 7-H of α-methyl isomer and 1 H, 7-H of β-methyl isomer), 4.09 (q, *J* = 7.02 Hz, OCH_2CH_3), 4.12−4.27 (m, 1 H, 6-H of α-methyl isomer and 1 H, 6-H of β-methyl isomer), 4.40 (br. s., 1 H, 5-H of one isomer), 4.49−4.54 (m, 1 H, 4-H of both isomers, 1 H, 5-H of one isomer), 7.38−7.77 (m, C_6H_5 of α- and β-methyl isomers) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.10 (CH_3, OCH_2CH_3), 19.48 (C_q, *t*Bu, TBDPS), 27.04 (*t*Bu, TBDPS), 45.37 and 46.72 (CH_2, C-3 of α- and β-methyl isomers), 51.95, 52.68, 53.12 (CO_2CH_3 of α- and β-methyl isomers and OCH_3 of α- and β-methyl isomers), 63.67, 64.10 and 65.30 (CH_2, C-8 of α- and β-methyl isomers, OCH_2CH_3), 72.04 and 72.70 (CH, C-6 of α- and β-methyl isomers), 73.12 and 73.32 (CH, C-4 of α- and β-methyl isomers), 73.81 and 74.05 (CH, C-7 of α- and β-methyl isomers), 80.50 and 83.36 (CH, C-5 of α- and β-methyl isomers), 105.66 (C_q, C-2 of α- and β-methyl isomers), 127.86, 130.03, 135.86 (CH, C_6H_5), 133.73, 135.69 (C_q, C_6H_5), 171.13 (C=O, CO_2CH_3) ppm. ^{31}P NMR (161 MHz, $CDCl_3$): δ = −0.15 ppm. MS (DCI, NH_3): *m/z* = 641 [M + H^+], 658 [M + NH_4^+]. $C_{30}H_{45}O_{11}SiP$ (640.7): calcd. C 56.24, H 7.08; found C 56.38, H 7.16.

X-ray Crystallographic Study. Crystal Data for 33a: $C_{34}H_{51.50}O_8Si_2$, *M* = 644.43, triclinic, space group *P*1. *a* = 7.6691(11), *b* = 11.5221(16), *c* = 21.715(3) Å, α = 84.823(3), β = 82.102(3), γ = 70.727(3)°, *V* = 1792.0(4) Å^3, *Z* = 2, $\rho_{calcd.}$ = 1.194 Mg·m^{-3}, *F*(000) = 695, λ = 0.71073 Å, *T* = 193(2) K, μ(Mo-K_α) = 0.145 mm^{-1}, crystal dimensions 0.2 × 0.4 × 0.5 mm, 1.87° ≤ θ ≤ 24.71°; 9224 reflections (7530 independent, R_{int} = 0.0617) were collected at low temperature from an oil-coated shock-cooled crystal with a Bruker-AXS CCD 1000 diffractometer. The structure was solved by direct methods (SHELXS-97), and 340 parameters were refined by the least-squares method on F^2.[29,30] Maximum residual electron density: 0.504 e/Å^3, *R*1 [for $F > 2\sigma(F)$] = 0.0515 and *wR*2 (all data) = 0.1267 with $R1 = |F_o| - |F_c|/|F_o|$ and $wR2 = w[(F_o^2 - F_c^2)^2/w(F_o^2)^2]^{0.5}$. Refinement of an inversion twin parameter [*x* = −0.16(9); *x* = 0 for the correct absolute structure and +1 for the inverted structure] confirmed the absolute structure of **33a**.[31] CCDC-187471 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments

We thank the CNRS and the "Ministère de l'Education Nationale de la Recherche et des Technologies" for financial support (UMR, 5068). C. H. S. and Y. R. acknowledge the "Ministère de l'Education Nationale de la Recherche et des Technologies" for postdoctoral and doctoral grants, respectively. We also thank H. Gornitzka of the "Service de Détermination Structurale par Diffraction des Rayons X sur monocristaux" and C. André for X-ray structure determination.

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Received July 12, 2002
[O02389]