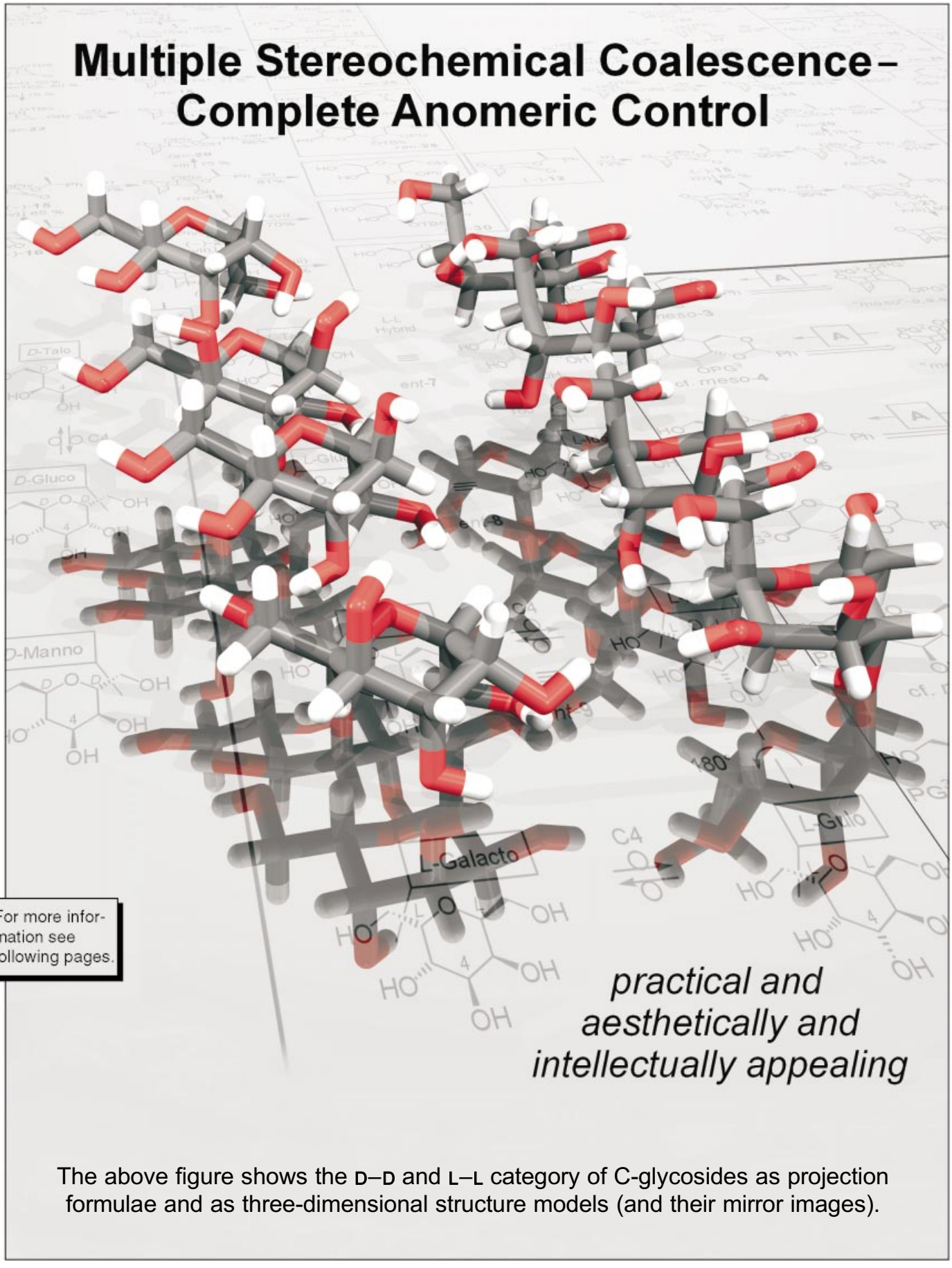
Multiple Stereochemical Coalescence–Complete Anomeric Control



For more information see following pages.

The above figure shows the D–D and L–L category of C-glycosides as projection formulae and as three-dimensional structure models (and their mirror images).

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The Total Synthesis of C-Glycosides with Completely Resolved Seven-Carbon Backbone Polyol Stereochemistry: Stereochemical Correlations and Access to L-Configured and Other Rare Carbohydrates

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Abstract: The de novo synthesis of a full set of hydroxymethyl C-glycosides from only two precursors is described. The *seven-carbon* target molecules contain five stereocentres and bridge the stereochemical gap between natural D-configured and non-natural L-configured series of hexoses. Key steps include hydroxylation, differential protection, stereoselective reduction and desymmetrization of 8-oxabicyclo[3.2.1]oct-6-enes. C-Terminus differentiation and C-terminus excision of the *seven-carbon* polyol backbone lead to hexoses, including those of the L-series. A stereochemical and genetic classification of C-glycosides is presented.

Keywords: carbohydrates · C-glycosides · cycloaddition · de novo syntheses · stereochemical coalescence

Introduction

Carbohydrates are essential molecules of biological systems.[1] They contribute to the structural framework of cells and tissues and play an important role as an energy storage system.[2] A high number of glycoconjugates,[3] such as glycoproteins and glycolipids, are involved in coding information and in cell–cell recognition.[4] They are built of oligosaccharide structures and a protein or lipid moiety and are located on the cell surface. The phantastic structural and stereochemical diversity of carbohydrates, also called the glycocode, exceeds that of polypeptides by far. While five different difunctional amino acids furnish 120 different pentamers of typ ABCDE, the number of corresponding pentameric structures of five different monosaccharides has been calculated to be 2 144 640.[5] Because of the essential role in cell–cell and cell–pathogen communication the development of new carbohydrate mimics for drug discovery or mechanistic explorations of cellular interactions and metabolism is promising.[6] In recent years C-glycosides[7] have been the focus of attention because of their more stable C-glycosidic linkage.[8] The most obvious application is to utilize them as inhibitors of glycosidases and transferases,[9] which are known to be involved in cancer, viral infections and metabolism defects.[10] So far C-glycosides of rare and non-natural sugars have been studied much less presumably because of lack of access. The eight L-configured open-chain aldohexoses (six-carbon atoms, four stereocentres) have been synthesized by Masamune and Sharpless, using the Sharpless AE reaction as key step.[11] Vogel and his colleagues have prepared a wide variety of sugars (and "naked sugars") starting from Diels–Alder adducts of furan.[12] Non-natural six-carbon sugars have also been synthesized more recently by Ogasawara from furfuraldehyde.[13]

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Concept—Correlations—Classification

We report the de novo synthesis of a full set of hybrid D- and L-C-glycosides starting with the unsaturated [3.2.1]oxabicyclic framework. The target molecules contain a fifth stereocentre in the six-membered oxacycle.

It occurred to us that a hybrid series of C-glycosides can be constructed consisting of the naturally occurring set of D-hexoses and the non-natural L-enantiomers: Such a series (with a progression from six to seven carbon atoms and five stereocentres) has structural and stereochemical features of both D- and L-configured pyranosides. Moreover in our case, the series is created from non-carbohydrate starting materials. We illustrate our plan with a gedanken experiment involving *meso*-configured C-glycosides **1**–**4** (Scheme 1).

Consider C-glycoside **1** which can be derived from D-talose, by β-selective hydroxymethylation of the D-talopyranose anomeric centre. Alternatively and completely independently, β-hydroxymethylation of the anomeric centre of non-natural L-talopyranose furnishes the identical seven-carbon D-L hybrid **1**. Hybrids **1**–**4** are achiral and correlate $2^4/2 = 8$

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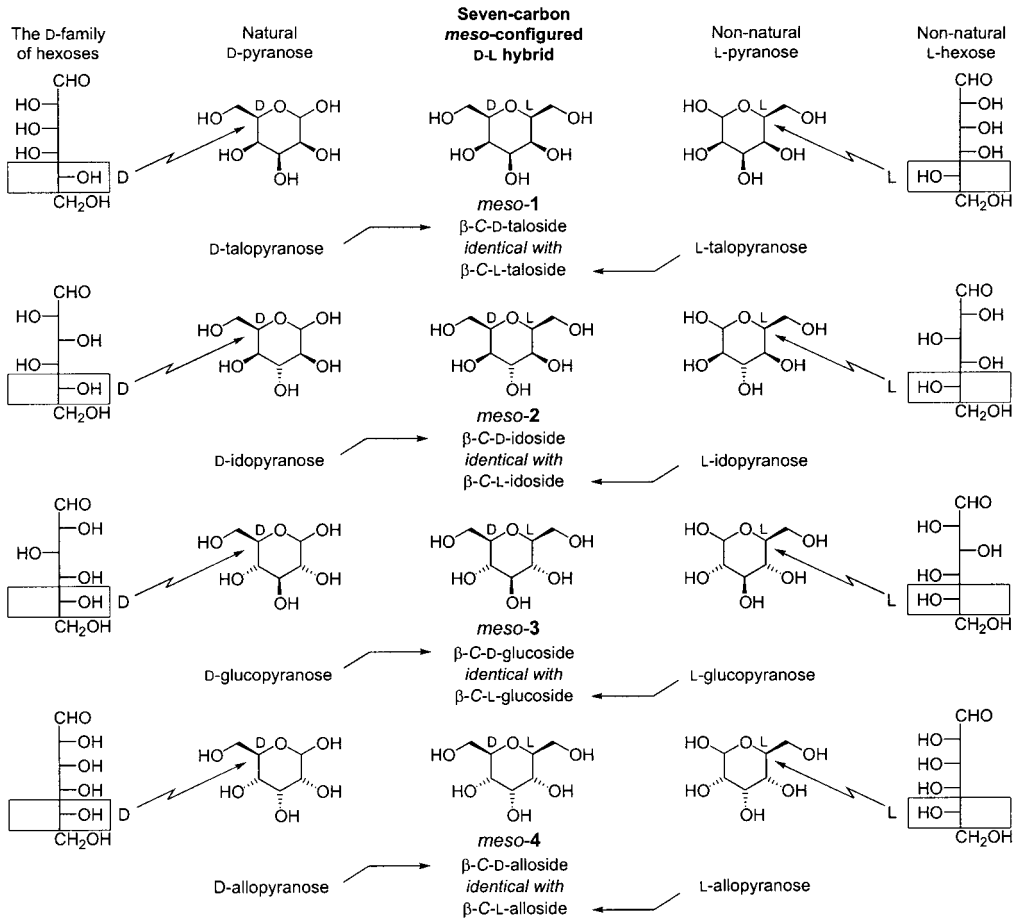
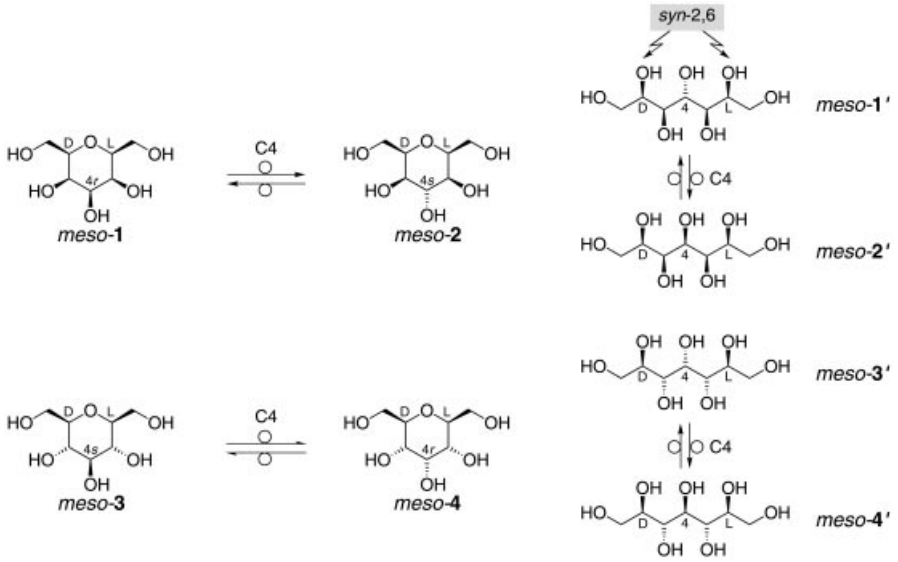


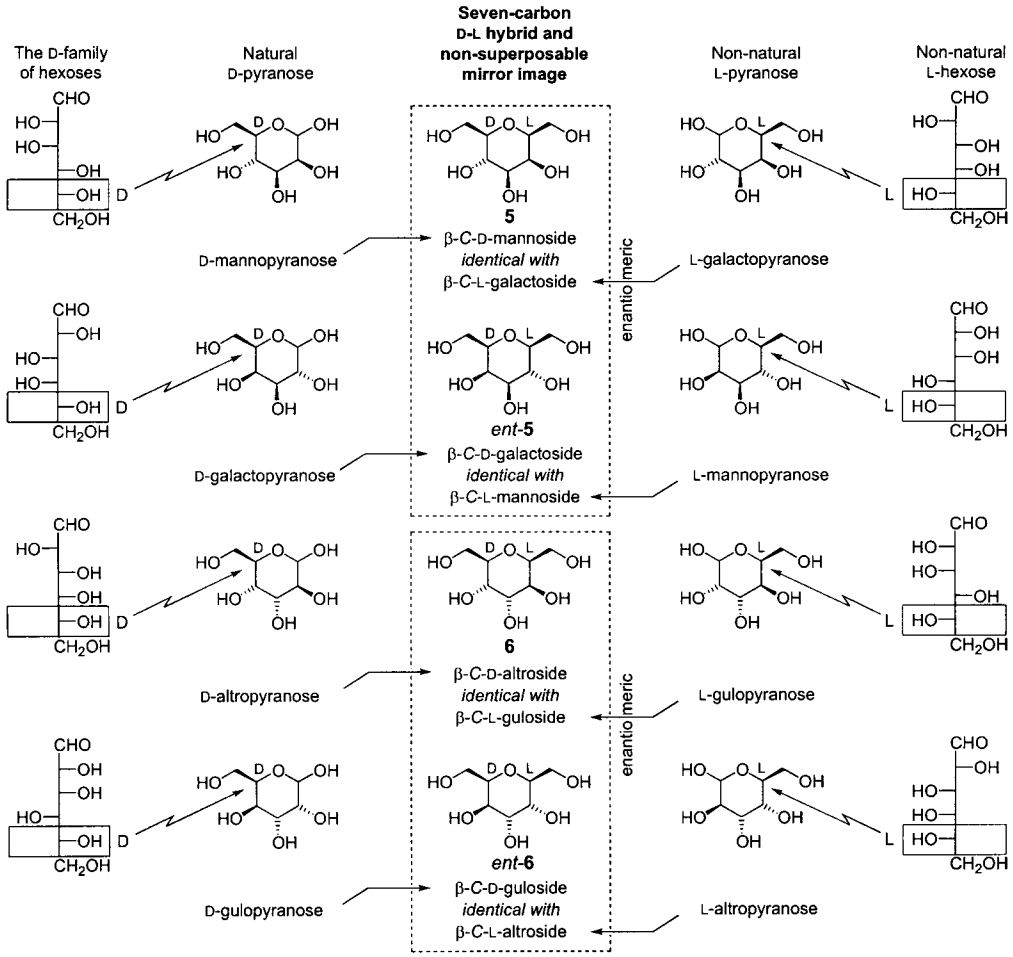
Scheme 1. β-Anomeric homologation of four pyranoside D and L pairs (first series): Symmetrization to *meso*-polyols.

stereoisomeric aldohexoses (D-allo-, D-gluco-, D-ido-, D-talopyranose with their respective L-enantiomer). In *meso*-**3** the five substituents attached to the tetrahydropyran ring are all-equatorial, just as in the β-D- and β-L-glucopyranose pair. The *meso* relationship is a powerful stereoconnector and allows further interrelations, namely by desymmetrization.

Furthermore, the carbon C4 is pseudo-asymmetric (Scheme 2) and is flanked by two substituents having identical *constitution*, but opposite *configuration*. According to the CIP rule[14] C4 has pseudo-asymmetry descriptor 4*r* in *meso*-**1**. A selective inversion (H, OH ligand interchange) transforms *meso*-**1** into its 4*s*-epimer *meso*-**2**, and *meso*-**3** into *meso*-**4** (Scheme 2). In theory, an inversion at central carbon C4 is a simple operation, but a number of experimental pitfalls had to be overcome. An attempted Mitsunobu inversion and a selective oxidation/reduction in a similar case (see below) were not successful, apparently because of the high oxygen atom density clustered around C4 and steric hindrance from various protecting groups. Eventually, conversion into the very reactive triflate and S_N2 inversion with tetra(*n*-butyl)ammonium nitrite (nBu$_4$NONO) was successful for a number of less hindered systems.



Scheme 2. Pseudo-asymmetry in *meso*-configured seven-carbon D-L hybrids and their open-chain equivalents with *syn*-2,6 stereochemistry.

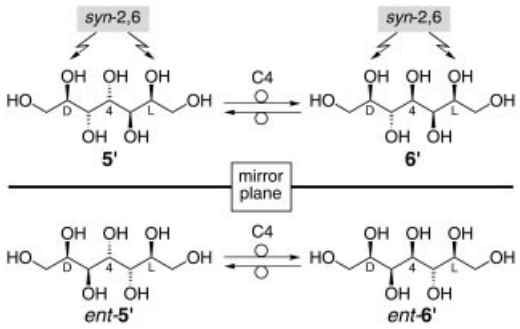


Scheme 3. β-Anomeric homologation of four further D and L pairs: Generation of two racemic pairs **5** and *ent*-**5**; **6** and *ent*-**6** (second series). C4 epimerization transforms **5** into **6** (*ent*-**5** into *ent*-**6**).

In our second series the remaining eight hexoses (D- and L-configured altro-, galacto-, gulo-, mannopyranose) are hydroxymethylated at the anomeric centre, again with exclusive β-stereoselection, generating two pairs of enantiomeric C-pyranosides, that is, **5** and *ent*-**5**; **6** and *ent*-**6** (Scheme 3). Thus, the stereochemical degeneracy and σ-symmetric structure of **1**–**4** (see Scheme 1) have disappeared.

Each C-glycoside in Scheme 3 can be regarded as a D-L hybrid of a D-hexose and a different single appropriate L-hexose. To exemplify, C-glycoside **5** is a β-hydroxymethylated C-D-mannoside and alternatively, a β-hydroxymethylated C-L-galactoside: The anomeric reference atom (=configuration defining atom) is D-configured in the mannoside core of **5** and L-configured in the galactoside core. C-Glycoside **6** and its enantiomer *ent*-**6** have been constructed accordingly (Scheme 3). The generation of four D-L hybrids (**5** and *ent*-**5**; **6** and *ent*-**6**) and the potential of further interconversions simplify organic syntheses substantially. In fact, the fully developed synthetic methodology for the second series comprises at most two non-enantiomeric stereoisomers.

In order to complete the series of seven-carbon hybrids, *homo*-chiral instead of *hetero*-chiral hexoses are paired, homologated and coalesced. In this case anomeric hydroxymethylation of eight D-aldopyranoses has to proceed stereoselectively from the α side, providing four D-D hybrids **7** to **10** with *trans*-configured hydroxymethyl groups. The corresponding set of four L-L hybrids is enantiomeric and consists of *ent*-**7** to *ent*-**10** (Scheme 5). The zig-zag chain seven-carbon equivalent polyols are listed in Scheme 6.[15] Schemes 1, 3 and 5 complete our D-L, D-D and L-L classification of C-glycosides, which focuses on the two key chiral centres C2 and C6. An assignment to any of these three classes can be made immediately on inspection of projection formulae. The notation allows us to spot genetic relationships with carbohydrates, while defining relative and absolute configuration at the penultimate positions C2 and C6.



Scheme 4. Open-chain polyol equivalents of second series with *syn*-2,6 relationship.

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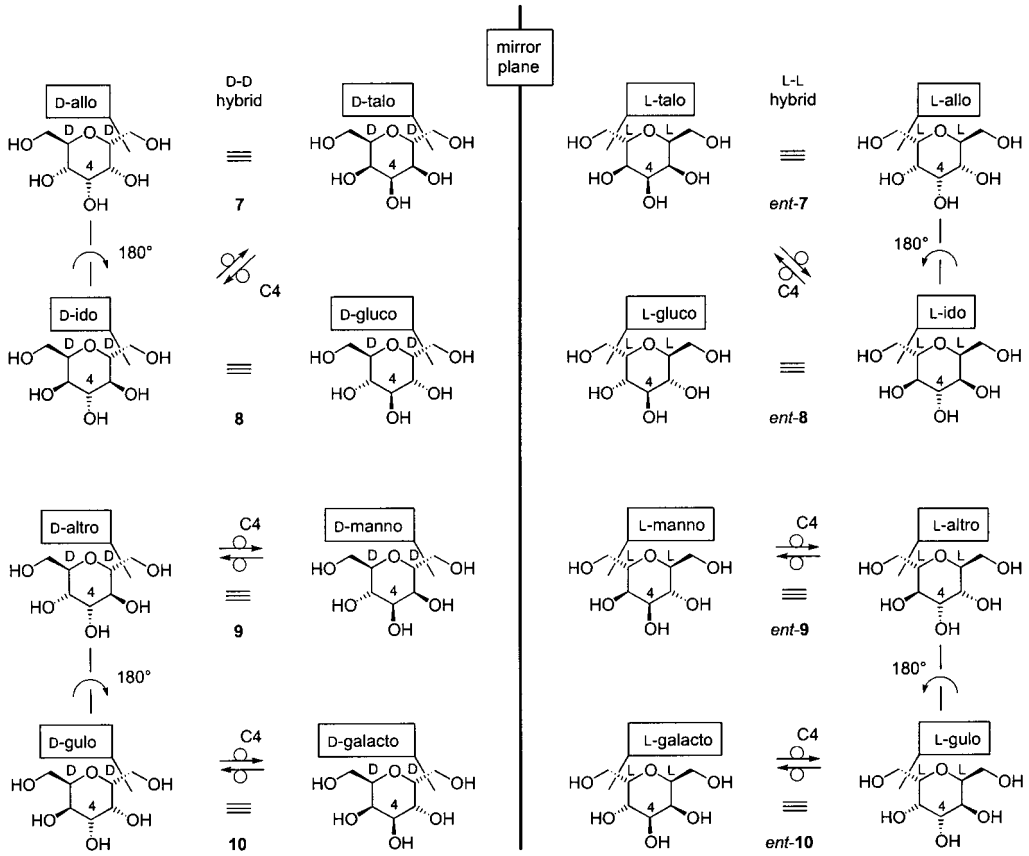
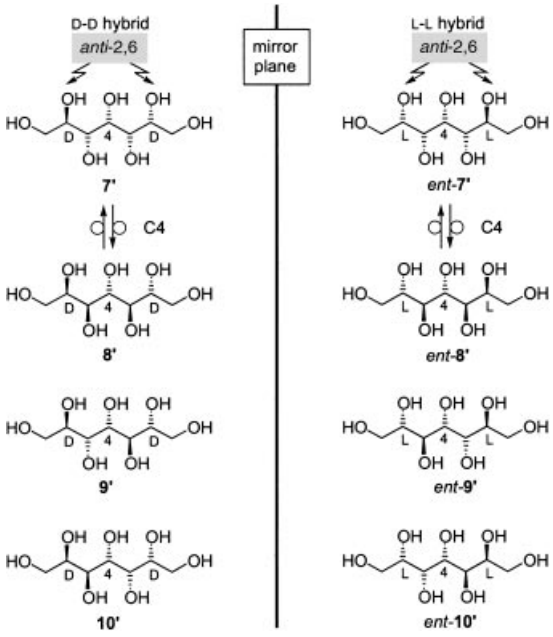


Scheme 5. Correlations of appropriate *homo*-chiral D-D and L-L pairs: Seven-carbon D-D and L-L hybrids with *anti*-2,6 relationship (third series). All molecules are C_2-symmetric. Stereoisomers **9**, *ent*-**9** (**10**, *ent*-**10**) are also invariant to inversion at carbon C4 (interchange of H and OH at C4 gives the identical molecule).



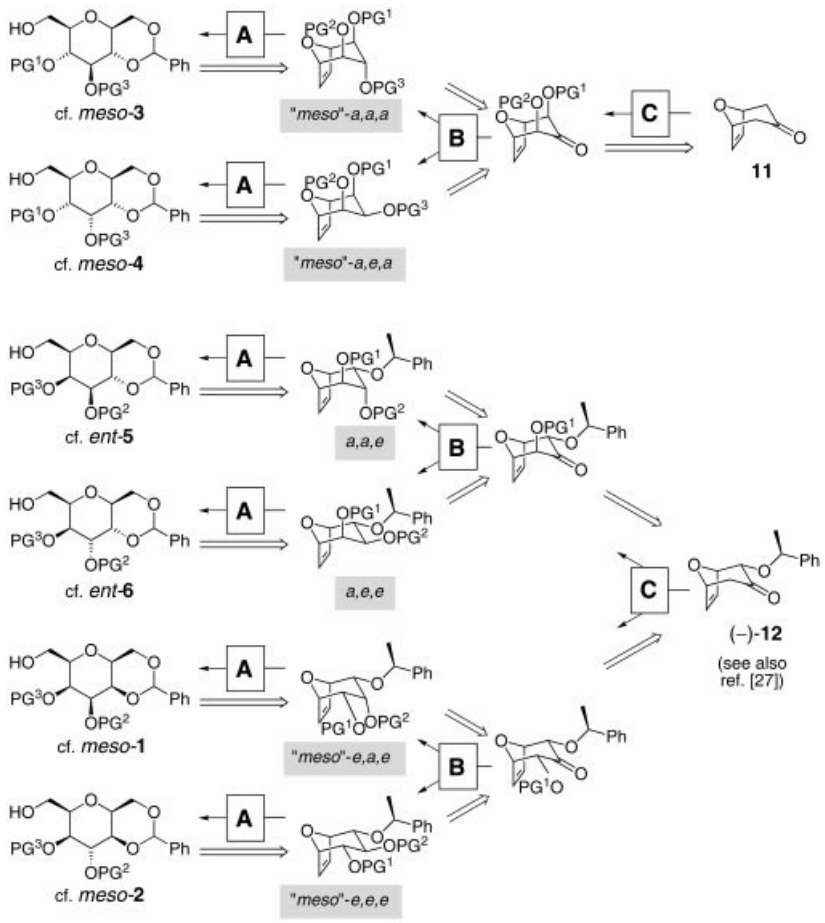
Scheme 6. Open-chain polyol equivalents: the D-D and L-L hybrids with *anti*-2,6 stereochemistry.

Total synthesis: A number of C-glycosides of Scheme 1, 3 and 5 have been reported in the past, although the polyhydroxy chain was not differentiated. Stereoisomer *meso*-**3**[16–19] (derived from D-glucose), D-D hybrid **8**[18–20] (from *meso*-**3** by L → D change), **5**,[17, 19] *ent*-**5**[19, 21] and *ent*-**6**[19] have been accessible. In each case a carbohydrate from the chiral pool was modified to provide the desired target.

Our retrosynthetic analysis starts from two simple bicyclic compounds, parent **11** and chiral α-oxygenated (−)-**12** (Scheme 7). Both **11** and (−)-**12** are conformationally constrained, but not entirely rigid, and they are to be elaborated by three key transformations: **A**, **B**, **C**. We planned to synthesize the C-glycosides in parallel fashion and with an orthogonal set of protecting groups.

Our first goal was to establish the oxygenation pattern and required stereochemistry around the carbonyl group which was to serve as fulcrum of these efforts. α-Hydroxylation (**Step C**) followed by stereoselective reduction (**Step B**) of the carbonyl moiety was considered as most practical approach. Ozonolysis (**Step A**) of the etheno bridge of a completely elaborated oxabicyclic precursor and subsequent reduction should allow anomeric control and provide the target molecules: *cis*-2,6-Configured hydroxymethyl groups are generated with relaxation of conformational constraint.

In practice [3.2.1]oxabicyclic ketone **11** was assembled via [4 + 3]-cycloaddition of furan with an allyl cation.[22] The recently developed asymmetric version of the cycloaddition, involving *chiral* carbocations as reactive intermediates, gave (−)-**12** in high enantiomeric purity.[23] Syntheses of both systems in multigram amounts have been described.

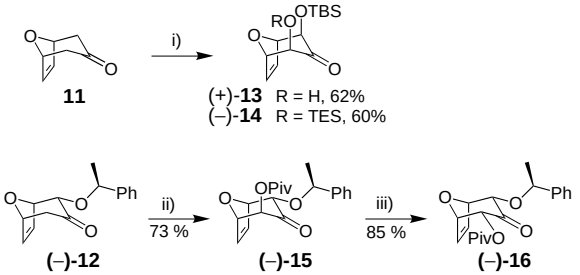


Scheme 7. Retrosynthetic plan. A: ozonolysis and differential protection (or alternative procedure), B: diastereoselective reduction, C: α-hydroxylation.

α-Hydroxylation of bicyclic ketones (Step C): We aimed at the preparation of all possible *tris*-hydroxylated oxabicyclic olefins, that is with *a*,*a*,*a*, *a*,*e*,*a*, *a*,*a*,*e*, *e*,*e*,*e*, *e*,*a*,*e* and *e*,*e*,*e* stereochemistry (Scheme 7). To our surprise, formation of *syn*-diaxial hydroxyketones (+)-**13** and (−)-**14** was straightforward, once a reliable hydroxylation procedure had been worked out. The silylenol ether[24] was prepared by in situ quench with chloro triethylsilane (TES-Cl)/lithium diisopropylamide (LDA) and oxidized with *meta*-chloroperbenzoic acid (*m*CPBA).[25] Equatorial epimers were not detected as oxidation products. A mixture of tetrahydrofuran and *water* 1:1 was essential to minimize side reactions. Under the optimized conditions regeneration of ketones by protonation of enolate intermediates was not observed. Tuning the silyl group (steric hindrance, steric stabilization and lipophilicity) showed that the triethylsilyl group (TES) is advantageous.[23] Excess of *m*CPBA may lead to epoxidation of the C6–C7 etheno bridge but was not detected when using 1.2 equiv *m*CPBA. TES-protected hydroxy ketone was the only major by-product. Simple addition of trifluoroacetic acid allowed desilylation. Applying this protocol to (−)-**12** as starting material gave, after acylation, the desired (−)-**15** in good yield. Efforts to establish the new hydroxy group (also equatorial) directly from (−)-**12** were unsatisfactory.[26] Eventually, basic epimerization of pivaloyl-protected (−)-**15** (but not acetyl protected analogue) and ultrasonication gave (−)-**16** in good yield.

At this point all possible α,α'-bis-hydroxylated ketones, that is (+)-**13** (*a*,*a*), doubly protected (−)-**14** (*a*,*a*) as well as (−)-**15** (*a*,*e*) and (−)-**16** (*e*,*e*) were available.[27] All hydroxylated ketones were obtained in high enantiomeric excess. All further transformations were equally stereoselective and carried out on enantio-enriched and also racemic materials, without loss of generality and with installation of the desired absolute and also relative stereochemistry (cf. also synthetic tree in Scheme 14).

Stereoselective reduction of carbonyl group (Step B): Usually [3.2.1]-bicyclic ketones such as (+)-**13**, (−)-**14** and (−)-**16** are selectively reduced by sterically demanding hydride donors from the more accessible side, furnishing the axial epimer at least predominantly.[28] For the 2,4-bis axial system reduction with L-Selectride or DIBAH gave mixtures of axial and equatorial alcohols. Intramolecular hydride transfer with $NaBH(OAc)_3$ provided the axially configured alcohol exclusively and in high yield.[29] Because of the high oxygen density on the upper side of the molecule a chelation-controlled reduction was envisioned as a route to equatorial epimer with hydride attack from the bottom face. In fact, reduction of (−)-**14** in presence of $MgBr_2$ proceeded under total stereocontrol: even $NaBH_4$ attacked from the bottom face.[30] Selective removal of the TES group provided (−)-**18** in excellent yield.[31]



Scheme 8. i) *n*BuLi, (+)-bis[(*R*)-1-phenylethyl]amine, TES-Cl/Et_3N (in situ quench), THF 88 %; *m*CPBA, THF/H_2O, 83 %; TBS-Cl, imidazole, CH_2Cl_2 99 %; LDA, TES-Cl/Et_3N (in situ quench), THF, 94 %; for R = H: 1) *m*CPBA, THF/H_2O, 2) TES-Cl/imidazole, CH_2Cl_2, 91 % (two steps); for R = TES: 1) *m*CPBA, THF/H_2O, 2) TFA, THF/H_2O, 88 % (two steps); ii) LDA, TES-Cl/Et_3N, THF, 98 %; *m*CPBA, THF/H_2O, 78 %; PivCl, Et_3N, DMAP, CH_2Cl_2, 95 %; iii) DBU, CH_3CN, ultrasound, 85 %.

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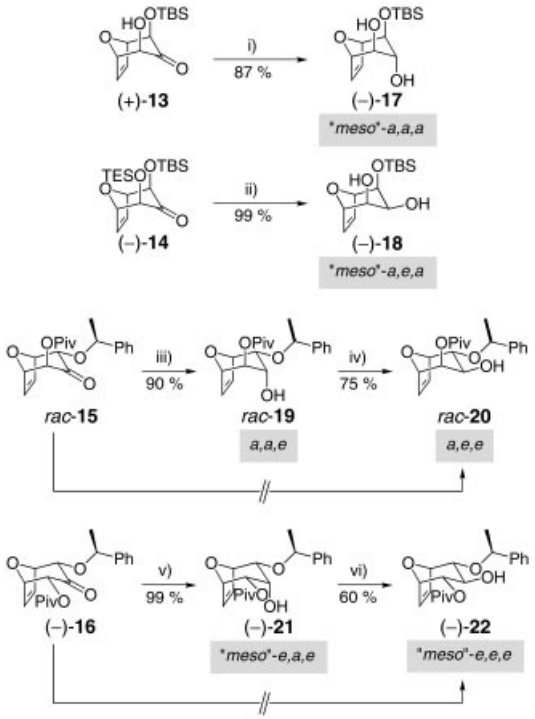
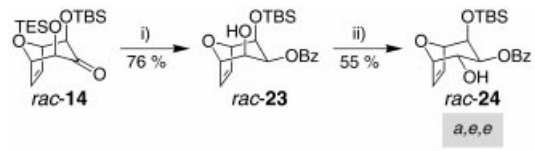
Attempts to obtain the *a*,*e*,*e* alcohol *rac*-**20** in one step from *rac*-**15** (cf. *rac*-**14** → *rac*-**18**) furnished exclusively the axial epimer *rac*-**19** in moderate yield, hydride ion attacking from the top. Adding $CeCl_3$ as chelation agent improved the yield to 90% with the same stereochemical result.[32] Numerous efforts to establish the equatorial stereochemistry at C3 through direct stereoselective reduction of ketone **15** failed. Finally it was found that the reaction of sensitive axially configured triflate with the sterically unhindered tetrabutylammonium nitrite (Bu_4NONO) as an effective nucleophile gave *rac*-**20** with complete inversion (S_N2).[33]

The same sequence succeeded for synthesizing both alcohols (−)-**21** and equatorial (−)-**22** from ketone (−)-**16** as starting material. Again, attempts at a stereoselective reduction of ketone (−)-**16** to *e*,*e*,*e*-configured (−)-**22** in one step failed.

As an alternative access to the *a*,*e*,*e*-stereochemistry of *rac*-**20** a stereoselective reduction of ketone (−)-**14** to the equatorial alcohol was carried out under chelation control giving (−)-**18**. Inversion of configuration at C2 (*rac*-**23** → *rac*-**24**) proceeded by the triflate/Bu_4NONO procedure as outlined in Scheme 10. The structure of *rac*-**20** and of (−)-**22** (both with equatorial C3-OH groups) was proven by X-ray crystal diffraction.[34] In an ancillary study the crystal structure of *syn*-diaxial **13** has also been determined.[35] The synthesis and essential chemistry of six key unsaturated oxabicyclic triols were now worked out. A masked *meso*-**1** equivalent (cf. (−)-**21**) had also been converted directly into a *meso*-**2** equivalent (cf. (−)-**22**) (Scheme 9). These and other secondary interconversions further reduce the number of essential intermediates en route to the target C-glycosides. In fact, since (−)-**12** has, in principle been transformed into **11** and vice versa the number of starting materials could be reduced to one *single* oxabicycle.

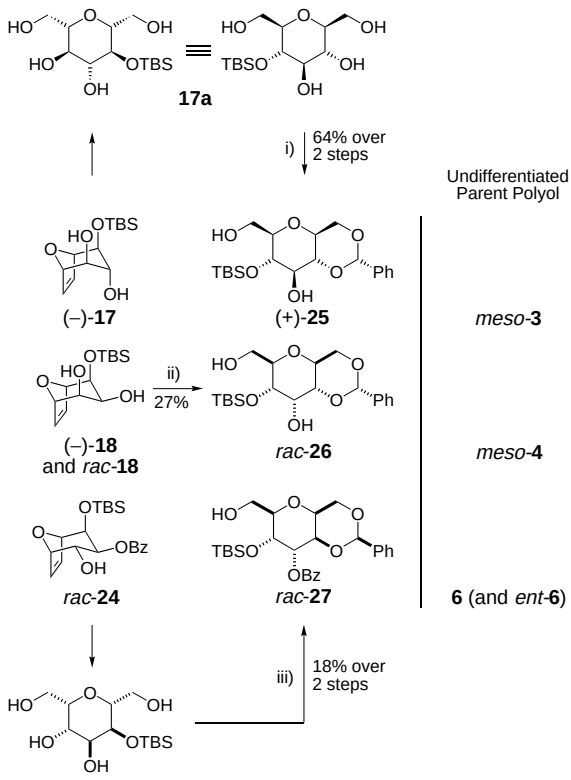


Scheme 9. Six key unsaturated triols from hydroxylated **11** and (−)-**12** in short synthetic order. i) $NaBH(OAc)_3$, THF/AcOH, 87%; ii) $NaBH_4$, $MgBr_2$, MeOH, 99%; TFA, THF/H_2O, 77%; iii) $NaBH_4$, $CeCl_3$, THF/EtOH, 90%; iv) 1) Tf_2O, py, DMAP, CH_2Cl_2; 2) Bu_4NONO, CH_2Cl_2, 75% (two steps); v) $NaBH_4$, $CeCl_3$, THF/EtOH, 99%; vi) 1) Tf_2O, py, DMAP, CH_2Cl_2, 2) Bu_4NONO, DMSO, 60% (two steps).



Scheme 10. Alternative route to *a*,*e*,*e*-triol. i) $NaBH_4$, $MgBr_2$, MeOH, 99%; BzCl, py, DMAP, 86%; TFA, THF/H_2O, 89%; ii) Tf_2O, py, DMAP, CH_2Cl_2, 80%; Bu_4NONO, DMF, 69%.

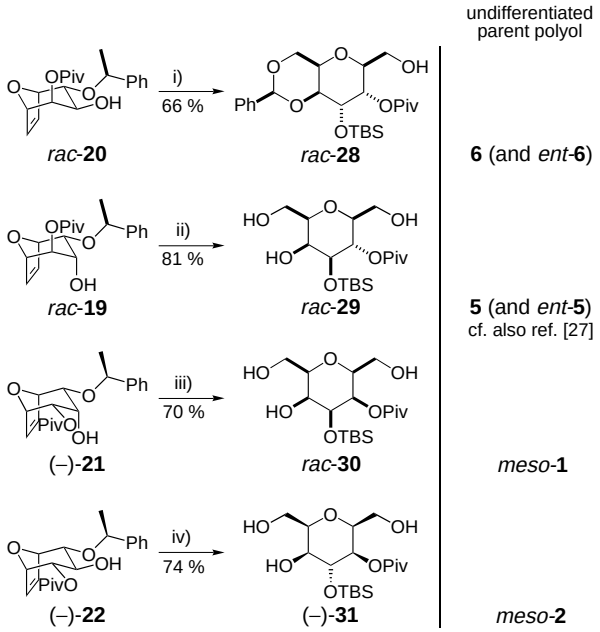
Oxidative opening of bicyclic framework to C-glycosides and carbohydrate mimics (Step A): For the alcohols (−)-**17**, *rac*-**18** and *rac*-**24** simple ozonolysis followed by reduction ($NaBH_4$) and formation of benzylidene acetal provided the target C-glycosides (+)-**25**, *rac*-**26**, *rac*-**27** with completely differentiated polyol backbone (see Scheme 11).[36]



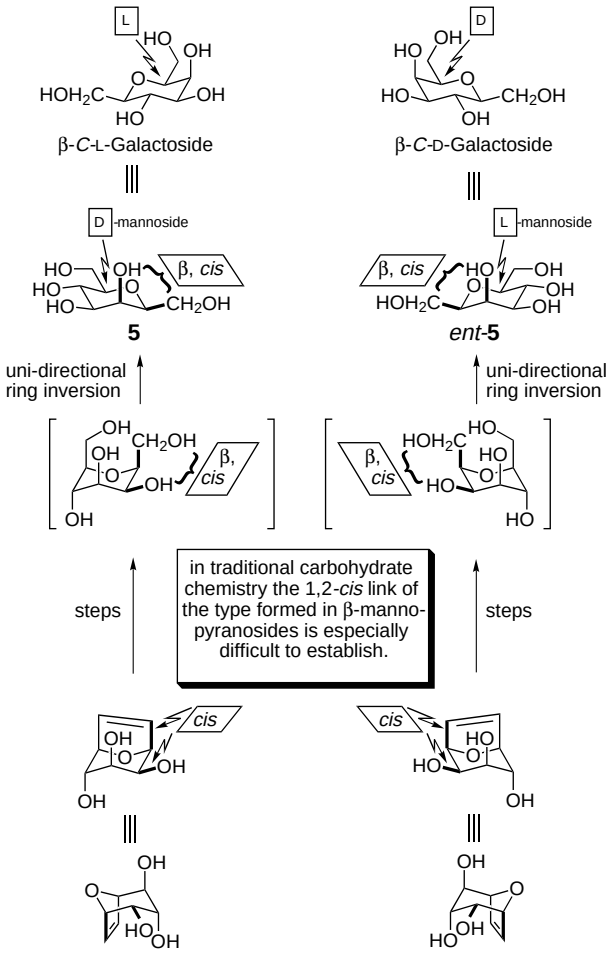
Scheme 11. i) O_3, $NaBH_4$, CH_2Cl_2/MeOH, 98%; *p*TsOH, $PhCH(OMe)_2$, CH_3CN, 36%; ii) O_3, $NaBH_4$, CH_2Cl_2/MeOH, 99%; PPTS, $PhCH(OMe)_2$, CH_2Cl_2, 64%; iii) O_3, $NaBH_4$, CH_2Cl_2/MeOH, 47%; *p*TsOH, $PhCH(OMe)_2$, CH_3CN, 39%. Solid and dashed wedges denote absolute stereochemistry, solid and broken joists give relative stereochemistry.

Similarly, the four oxabicyclic systems *rac*-**19**, *rac*-**20**, *rac*-**21** and (−)-**22** were opened by ozonolysis after protection as TBS-ethers. Removal of the 1-phenylethyl protecting group by Pd-mediated hydrogenolysis led to the triols *rac*-**29**, *rac*-**30** and (−)-**31**. With *rac*-**20** as starting material the final

protection as benzylidene acetal afforded *rac*-**28** as shown (Scheme 12). There was no re-symmetrization. Because of the orthogonally protected hydroxy groups the seven-carbon backbone remains chiral and non-racemic.



Scheme 12. i) TBS-Cl, imidazole, DMF, 93 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 90 %; $Pd(OH)_2$/C, EtOH, H_2, 93 %; $PhCH(OMe)_2$, *p*TsOH (cat.), CH_3CN, 85 %; ii) TBS-Cl, imidazole, DMF, 95 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 91 %; $Pd(OH)_2$/C, EtOH, H_2, 94 %; iii) TBS-Cl, imidazole, DMF, 84 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 89 %; $Pd(OH)_2$/C, EtOH, H_2, 94 %; iv) TBS-Cl, imidazole, DMF, 85 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 92 %; $Pd(OH)_2$/C, EtOH, H_2, 95 %.



Scheme 13. Synthesis of the β-C-mannopyranosides **5** and *ent*-**5**: To help locating the embedded mannosyl (and galactosyl) moiety and the alternating anomeric centres of the seven-carbon polyols, the "unnatural hydroxymethyl group" has been drawn as CH_2OH (see also Scheme 3).

Although the three-dimensional perspective is subdued, we have frequently used the Mills projection formulae to illustrate configurational relationships. With puckered rings three-dimensional features are more apparent (Scheme 13). In conventional carbohydrate chemistry the construction of the 1,2-*cis* link of β-mannopyranosides is especially difficult.[37] In our approach ring-strain of the oxabicyclic precursor is released upon cleavage of the etheno double bond with uni-directional ring inversion. The usual anomeric effect is irrelevant and the β,*cis*-mannoside problem is solved almost en passant: both **5** and also *ent*-**5**, are obtained with "clean" stereochemistry (Scheme 13).

Perspectives—Conclusion—Modus Operandi

We have shown previously that [3.2.1]oxabicycles are multiple aldol addition equivalents for a wide range of complex tetrahydropyrans characteristic of marine natural products. Furthermore, parallel chemistry has created high-quality polyketide segments which are individually separable.[38]

The present strategy is concise and yet can be relied on to fashion a wide range of C-glycosides. Only two oxabicyclics have been used as seven-carbon polyol building blocks. Sequential oxygenation of the three-carbon bridge provides densely functionalized molecules with completely resolved oxygen functions (Scheme 14). The pro-stereogenic two-carbon unsaturated bridge is synthetically versatile and has been modified and elaborated in various ways. Ozonolysis "through the middle" and subsequent reduction (Schemes 11 – 14) furnish two *cis*-configured hydroxymethyl groups. The end groups have been differentiated by intramolecular acetalization.

Earlier, enantiotopic *cis*-2,6-bishydroxymethyl groups were recognized enzymatically as described for a ring B bryostatin synthesis.[39]

A further option has been developed in the synthesis of the Southern segment of lasonolide A C1−C16 and is adumbrated in Scheme 15. After oxidative cleavage either one silylated hydroxy ester [step v(1)] or the constitutional isomer [step v(2)] with interchanged ester and hydroxy functionality have been prepared.[38, 40]

The synthesis of D-D and of the much less common L-L configured C-glycosides of the third series requires a single inversion at C6 or C2. We have shown previously that [3.3.1]lactone acetals as a new class of compounds are

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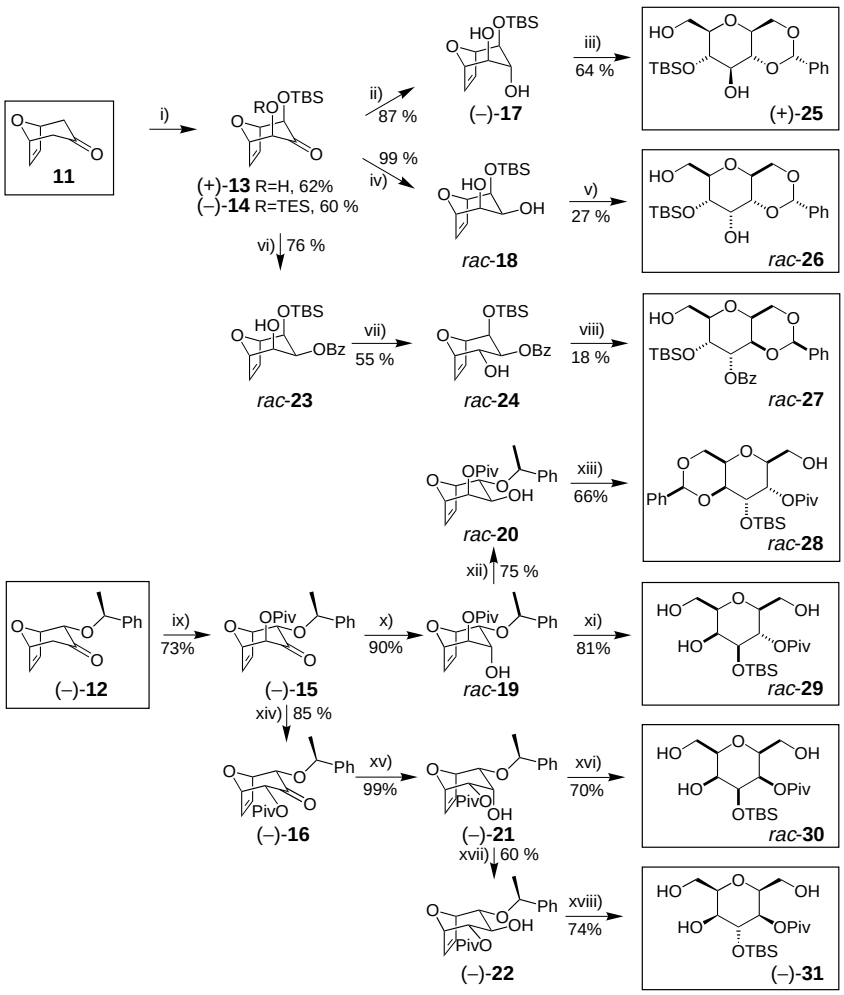


Scheme 14. Linear and parallel steps *en route* to hybrid C-glycosides. In the later stages of the synthesis racemic but diastereomerically pure substrates and achiral reagents were used, without loss of relative stereochemistry. Furthermore, both (–)-**12** and its enantiomer (+)-**12** have been synthesized previously (ref. [23]). i) *n*BuLi, (+)-bis[(*R*)-1-phenylethyl]amine, TES-Cl/Et_3N (in situ quench), THF 88 %; *m*CPBA, THF/H_2O, 83 %; TBS-Cl, imidazole, CH_2Cl_2 99 %; LDA, TES-Cl/Et_3N (in situ quench), THF, 94 %; for R = H: 1) *m*CPBA, THF/H_2O, 2) TES-Cl/imidazole, CH_2Cl_2 91 % over two steps; for R = TES: 1) *m*CPBA, THF/H_2O, 2) TFA, THF/H_2O, 88 % over two steps; ii) $NaBH(OAc)_3$, THF/AcOH, 87 %; iii) O_3, $NaBH_4$, CH_2Cl_2/MeOH, 99 %; PPTS, $PhCH(OMe)_2$, CH_2Cl_2, 64 %; iv) $NaBH_4$, $MgBr_2$, MeOH, 99 %; TFA, THF/H_2O, 77 %; v) O_3, $NaBH_4$, CH_2Cl_2/MeOH, 98 %; *p*TsOH, $PhCH(OMe)_2$, CH_3CN, 36 %; vi) $NaBH_4$, $MgBr_2$, MeOH, 99 %; BzCl, py, DMAP, 86 %; TFA, THF/H_2O, 89 %; vii) Tf_2O, py, DMAP, CH_2Cl_2, 80 %; Bu_4NONO, DMF, 69 %; viii) O_3, $NaBH_4$, CH_2Cl_2/MeOH, 47 %; *p*TsOH, $PhCH(OMe)_2$, CH_3CN, 39 %; ix) LDA, TES-Cl/Et_3N (in situ quench), THF, 98 %; *m*CPBA, THF/H_2O, 78 %; PivCl, Et_3N, DMAP, CH_2Cl_2, 95 %; x) $NaBH_4$, $CeCl_3$, THF/EtOH, 90 %; xi) TBS-Cl, imidazole, DMF, 95 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 91 %; $Pd(OH)_2$/C, EtOH, H_2, 94 %; xii) 1) Tf_2O, py, DMAP, CH_2Cl_2; 2) nBu_4NONO, CH_2Cl_2, 75 % over two steps; xiii) TBS-Cl, imidazole, DMF, 93 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 90 %; $Pd(OH)_2$/C, EtOH, H_2, 93 %, $PhCH(OMe)_2$, *p*TsOH (cat.), CH_3CN, 85 %; xiv) DBU, CH_3CN, ultrasound, 85 %; xv) $NaBH_4$, $CeCl_3$, THF/EtOH, 99 %; xvi) TBS-Cl, imidazole, DMF, 84 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 89 %; $Pd(OH)_2$/C, EtOH, H_2, 94 %; xvii) 1) Tf_2O, py, DMAP, CH_2Cl_2, 2) Bu_4NONO, DMSO, 60 % over two steps; xviii) TBS-Cl, imidazole, DMF, 85 %; O_3, $NaBH_4$, CH_2Cl_2/MeOH, 92 %; $Pd(OH)_2$/C, EtOH, H_2, 95 %.

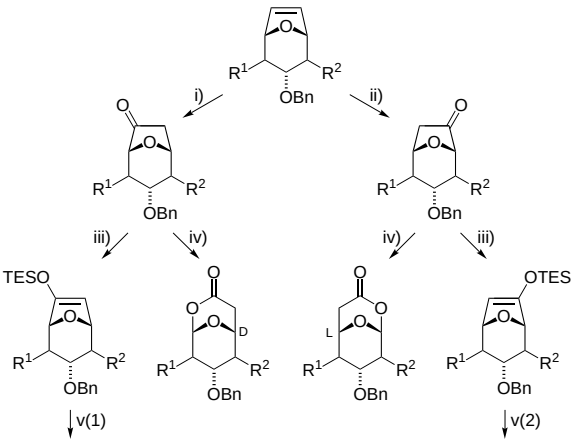
excellent glycosyl donors. One bridgehead carbon is anomeric (either D or L) in the conventional sense with uniformly high yields in the C-glycosidation reaction (ca. 95 %) (Scheme 16). Consequently, both D-D type and L-L type C-glycosides are also readily accessible, the nucleophile being introduced *trans* to the glycosidic linkage with excellent stereoselectivity. Moreover, glycosyl cyanides (D-D) have been prepared. The change from D-D back to D-L hybrid occurs on base-induced epimerization.[38, 41] Various transitions within the general D-L, D-D and L-L frame have been effected experimentally. An activated leaving group is not necessarily required for glycosylation: Even tetrahydropyran acetals with methoxide ion as supposedly poor leaving group serve as glycosyl donors[42] in acetonitrile. It is of biogenetic and general interest that naturally occurring C-linked glycosides belonging to the L-L category, but outside the conventional carbohydrate area, are also rare. An example is the marine metabolite phorboxazole[43, 44] with its C4 – C10 substructure which we prepared from universal 8-oxabicyclo[3.2.1]oct-6-en-3-one (**11**)[28b, 41b] and also halichondrin B (C5 – C11 and C28 – C34 segment).[45] More recently apicularen[46] has been isolated from myxobacteria.[47] Phorboxazole, the halichondrins and apicularen are potent anticancer agents suggesting that fine-tuning of L-L tetrahydropyran stereochemistry and shape contribute to bioactivity.

Reversion from seven carbon atoms to six carbon atoms yields traditional D-configured carbohydrates and their L-enantiomers via directed C-terminus excision, by known free radical and ionic methodology (Schemes 16, 17). In each case, four of the original five stereocentres of the carbon backbone remain untouched.

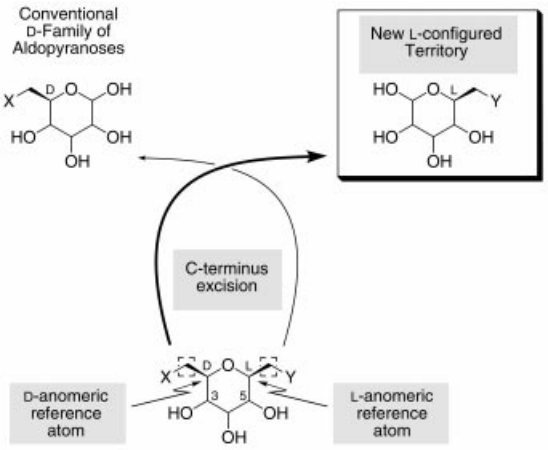
In summary, multiple stereochemical coalescence by pairwise stereoselective homologation is a powerful principle for organic synthesis. Exceedingly simple solutions for stereocontrolled syntheses of complex polyfunctionalized materials, C-glycosides and carbohydrates including rare and non-natural species are within experimental reach.

Experimental Section

Note: For reasons of readability the numbering of bicyclic systems follows the order of hydroxylation instead of the usual priority rules. The numbering of the tetrahydropyrans follows IUPAC rules.

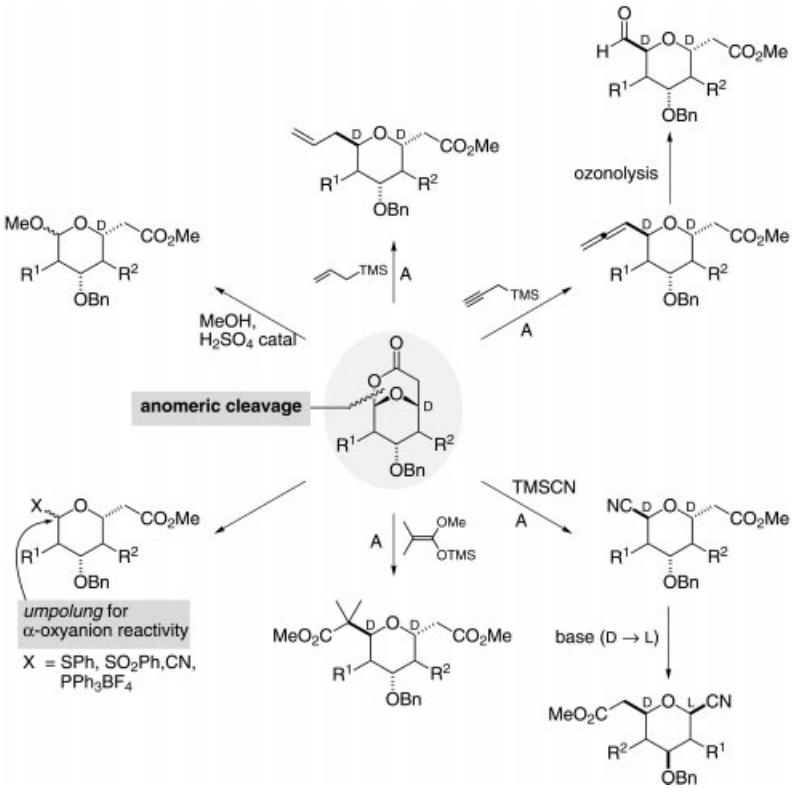


Scheme 15. D- and L-Configured glycosyl donors from 8-oxabicyclo[3.2.1]oct-6-en-3-ones. i) (−)-Ipc_2BH; oxidation; ii) (+)-Ipc_2BH; oxidation; iii) LDA, TES-Cl/NEt_3 (in situ quench), THF, −78 °C, 1 h; iv) *m*CPBA; v(1) and v(2): ozonolysis, $NaBH_4$.

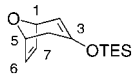


Scheme 17. C-Terminus differentiation and C-terminus excision in seven-carbon D-L configured glycosyl donors. For simplicity the stereochemistry at C3, C4, C5 and all protecting groups are omitted. In the most simple case $CH_2X \triangleq CH_2Y = CH_2OH$. C-Terminus differentiation may be simpler for other combinations of end groups, e.g. CH_2OH and $CO_2H/CO_2R/CN/CONH_2/CHO$ (see also Schemes 15, 16).

General methods: Infrared spectra were recorded on a Perkin–Elmer 1710 IR spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 400 spectrometer in deuterated chloroform unless otherwise stated, with tetramethylsilane as internal standard. Mass spectra were recorded on a Finnigan MAT 312 (70 eV) or a VG Autospec spectrometer at RT unless otherwise stated. Preparative column chromatography was performed on J. T. Baker silica gel (particle size 30–60 μm). Analytical TLC was carried out on aluminium-backed 0.2 mm silica gel 60 F_{254} plates (E. Merck). THF was distilled over sodium/benzophenone before use. CH_2Cl_2 was distilled over CaH_2 before use. DMF was dried over BaO and distilled over CaH_2 before use. Methyl *tert*-butyl ether (MTBE), diethyl ether (E), ethyl acetate (EA), cyclohexane (CH) and light petroleum ether (PE, b.p. 40–60 °C) were distilled before use.



Scheme 16. Stereoselective synthesis of C-glycosides with D-D type configuration. A: All reactions were run with TMSOTf (ca. 1 equiv) in CH_3CN, −40 → 0 °C; then addition of MeOH, RT → in situ esterification. Yields uniformly ca. 95%. L-L type C-glycosides are accessible from L-anomeric [3.3.1]lactone acetal (cf. Scheme 15 and refs. [41], [42]).



(1*R*,5*R*)-3-Triethylsilanyloxy-8-oxabicyclo[3.2.1]octa-2,6-diene [(+)-11a]: (+)-Bis[(*R*)-1-phenylethyl]amine (20.88 g, 92.74 mmol) was added to a suspension of LiCl(2.06 g, 42.5 mmol) in THF (300 mL). *n*BuLi (55.4 mL, 88.7 mmol, 1.6 M in hexane) was added slowly at −100 °C. After 5 min the reaction mixture was allowed to warm to RT and was stirred for 20 min at RT. A previously prepared solution of 8-oxabicyclo[3.2.1]oct-6-en-8-one (**11**; 10 g, 81 mmol) in THF (100 mL) was added dropwise at −100 °C over a period of 1 h followed by a mixture of triethylamine (28.0 mL, 202 mmol) and TES-Cl (16.2 mL, 96.8 mmol). After being stirred at −100 °C for 30 min the reaction mixture was allowed to warm to RT and was poured into an ice-cold sat. $NaHCO_3$ solution. After extraction with MTBE the combined organic layers were dried ($MgSO_4$), the solvent was removed and the resulting oil was purified by flash chromatography (CH/MTBE) giving (+)-**11a** (16.92 g, 88%)as a colourless oil. The enantiomeric excess was determined after preparation of (−)-**11b** by NMR-shift measurement and was found to be 83% *ee*. $[\alpha]_D^{20} = +44.6$ ($c = 1$, $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 6.47$ (dd, $J = 5.9$, 1.7 Hz, 1H; H-6), 5.92 (dd, $J = 5.9$, 1.9 Hz, 1H; H-7), 5.22 (dt, $J = 4.8$, 1.3 Hz, 1H; H-2), 4.92 (dd, $J = 6.3$, 1.8 Hz, 1H; H-5), 4.79 (m, 1H; H-1), 2.63 (ddt, $J = 17.3$, 6.1, 1.2 Hz, 1H; H-4_{ax}), 1.68 (dd, $J = 17.3$, 0.7 Hz, 1H; H-4_{eq}), 0.95 (t, $J = 8.0$ Hz, 9H; $Si(CH_2CH_3)_3$), 0.64 (q, $J = 8.0$ Hz, 6H; $Si(CH_2CH_3)_3$); ^{13}C NMR ($CDCl_3$): $\delta =$ 147.29 (C_q, C-3), 137.95 (CH, C-6), 126 (CH, C-7), 107 (CH, C-2), 76.87 (CH, C-5), 75.06 (CH, C-1), 32.70 (CH_2, C-4), 6.57 (CH_3, $Si(CH_2CH_3)_3$), 4.95 (CH_2, $Si(CH_2CH_3)_3$); IR (neat): $\tilde{\nu} = 2956$, 2912, 2876, 1640, 1460, 1416, 1352, 1308, 1256, 1240, 1200, 1056, 1016, 968, 944, 914, 868, 744 cm^{-1}; MS (rt): *m*/*z* (%): 238 (9) $[M]^+$, 223 (1), 209 (100), 195 (2), 179 (16), 151 (24), 116 (26), 103 (10), 87 (58).

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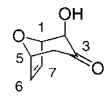
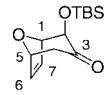
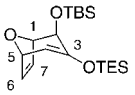


(1*R*,2*R*,5*R*)-2-Hydroxy-8-oxabicyclo-[3.2.1]oct-6-en-3-one [(−)-11b]: *m*CPBA (70%) (5.50 g, 37.7 mmol) was added at 0°C to a solution of (+)-**11a** (5.19 g, 22.0 mmol) in THF/H_2O (1:1, 66 mL). The mixture was stirred vigorously for 10 min, allowed to warm to RT and kept stirring for 2.5 h. After cooling to 0°C trifluoroacetic acid (1.7 mL, 22 mmol) was added. After complete reaction the resulting mixture was quenched by adding sat. $NaHCO_3$ solution and neutralized. The aqueous layer was saturated with solid NaCl and was extracted (EA). The combined organic layers were dried (Na_2SO_4) and the solvent was removed under reduced pressure. Flash chromatography (CH/EA) provided (−)-**11b** (2.6 g, 83%) as a white solid. $[\alpha]_D^{20} = -93.2$ ($c = 1$, $CHCl_3$); m.p. 46–48°C; ^{1}H NMR ($CDCl_3$): $\delta = 6.40$ (ddd, $J = 6.3$, 1.8, 0.7 Hz, 1H; H-6), 6.21 (dd, $J = 6.1$, 1.8 Hz, 1H; H-7), 5.03 (m, 1H; H-5), 4.94 (s, 1H; H-1), 3.70 (s, 1H; H-2), 3.05 (dd, $J = 16.6$, 5.0 Hz, 1H; H-4_{ax}), 2.32 (d, $J = 16.4$ Hz, 1H; H-4_{eq}); ^{13}C NMR ($CDCl_3$): $\delta = 204.87$ (C_q, C-3), 137 (CH, C-6), 133.56 (CH, C-7), 82.30 (CH, C-1), 77.32 (CH, C-5), 75.32 (CH, C-2), 44.47 (CH_2, C-4); IR ($CHCl_3$): $\tilde{\nu} = 3556$, 3040, 2968, 1728, 1376, 1332, 1228, 1032, 976, 844 cm^{-1}; MS: *m*/*z* (%): 140 (50) $[M]^+$, 122 (5), 111 (6), 98 (27), 97 (37), 81 (100).

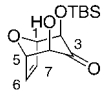


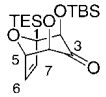
(1*R*,2*R*,5*R*)-2-(*tert*-Butyldimethylsilanyloxy)-8-oxabicyclo[3.2.1]oct-6-en-3-one [(−)-11c]: Imidazole (1.21 g, 17.9 mmol) was added at 0°C to a solution of (−)-**11b** (1.67 g, 11.9 mmol) in CH_2Cl_2 (25 mL) followed by TBS-Cl (2.16 g, 14.3 mmol). After being stirred for 30 min at 0°C the mixture was allowed to warm to RT and stirring was continued overnight. The reaction mixture was poured into a mixture of H_2O and E and was extracted with E. The combined organic layers were dried ($MgSO_4$) and the solvent was removed. Flash chromatography (CH/EA) gave (−)-**11c** (3.02 g, 99%) as a colourless oil. $[\alpha]_D^{20} = -36.3$ ($c = 1$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 6.37$ (dd, $J = 6.2$, 1.8 Hz, 1H; H-6), 6.14 (dd, $J = 6.0$, 1.8 Hz, 1H; H-7), 4.97 (br d, $J = 4.9$ Hz, 1H; H-5), 4.78 (br s, 1H; H-1), 3.64 (s, 1H; H-2), 3.03 (dd, $J = 15.9$, 4.8 Hz, 1H; H-4), 2.25 (d, $J = 15.9$ Hz, 1H; H-4_{eq}), 0.89 (s, 9H; $SiC(CH_3)_3$), 0.12 (s, 3H; $SiCH_3$), 0.05 (s, 3H; $SiCH_3$); ^{13}C NMR($CDCl_3$): $\delta = 203.96$ (C_q, C-3), 136.93 (CH, C-6), 129.52 (CH,C-7), 83.04 (CH, C-1), 77.22 (CH, C-5), 75.69 (CH,C-2), 45.00 (CH_2, C-4), 25.62 (CH_3, $SiC(CH_3)_3$), 18.21 (C_q, $SiC(CH_3)_3$), −4.86 (CH_3, $SiCH_3$), −5.01 (CH_3, $SiCH_3$); IR (neat): $\tilde{\nu} = 2956$, 2928, 2888, 2856, 1724, 1472, 1404, 1360, 1332, 1252, 1180, 1136, 1100, 1060, 1008, 988, 940, 916, 856, 836, 780 cm^{-1}; MS: *m*/*z* (%): 254 (5) $[M]^+$, 197 (4), 171 (4), 147 (7), 129 (100), 101 (3), 81 (4), 73 (15); HRMS: calcd for $C_{13}H_{22}O_3Si$: 254.1338, found: 254.1338.



(1*R*,2*R*,5*S*)-2-(*tert*-Butyldimethylsilanyloxy)-3-triethylsilanyloxy-8-oxabicyclo[3.2.1]octa-3,6-diene [(−)-11d]: *n*BuLi (12.24 mL, 19.58 mmol, 1.6 M in hexane) was added at −78°C to a solution of diisoproylamine (2.71 mL, 19.3 mmol) in THF (20 mL). The reaction mixture was stirred at RT for 20 min. A previously prepared mixture of triethylamine (4.99 mL, 35.8 mmol) and TES-Cl (3.81 mL, 22.7 mmol) was added slowly followed by a solution of (−)-**11c** (3.50 g, 13.8 mmol) in THF (21 mL). After 10 min the reaction was quenched by addition of sat. NH_4Cl solution at −78°C. After being warmed to RT the mixture was extracted (EA) and the combined organic layers were washed with brine, dried ($MgSO_4$) and the solvent was removed. Flash chromatography (CH/EA) provided (−)-**11d** (4.78 g, 94%)as a colourless oil. ^{1}H NMR ($CDCl_3$): $\delta = 6.68$ (dd, $J = 5.9$, 1.1 Hz, 1H; H-6), 6.03 (dd, $J = 5.9$, 2.0 Hz, 1H; H-7), 5.27 (d, $J = 4.8$ Hz, 1H; H-4), 4.81 (dd, $J = 4.6$, 1.8 Hz, 1H; H-5), 4.74 (d, $J = 2.0$ Hz,1H; H-1), 3.52 (s, 1H; H-2), 0.94 (t, $J = 7.8$ Hz, 9H; $Si(CH_2CH_3)_3$), 0.93 (s, 9H; $SiC(CH_3)_3$), 0.69 (q, $J = 7.8$ Hz, 6H; $Si(CH_2CH_3)_3$), 0.13 (s, 3H; $SiCH_3$), 0.12 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 147.67$ (C_q, C-3), 143.09 (CH, C-7), 125.98 (CH, C-6), 108.63 (CH, C-4), 84.93 (CH, C-5), 75.47 (CH, C-1), 69.74 (CH, C-2), 25.90 (CH_3, $SiC(CH_3)_3$), 18.34 (C_q, $SiC(CH_3)_3$), 6.55 (CH_3, $Si(CH_2CH_3)_3$), 4.86 (CH_2, $Si(CH_2CH_3)_3$), −4.29 (CH_3, $SiCH_3$), −4.90 (CH_3, $SiCH_3$); IR (neat): $\tilde{\nu} = 2956$, 2936, 2876, 2856, 1636, 1460, 1412, 1360, 1316, 1248, 1212, 1108, 1060, 1004, 984, 960, 944, 916, 876, 860, 836, 744 cm^{-1}; MS: *m*/*z* (%): 368 (30) $[M]^+$, 339 (14), 311 (35), 253 (6), 243 (29), 207 (6), 189 (17), 179 (24), 161 (23), 151 (17), 133 (9), 115 (93), 105 (9), 87 (100), 73 (73).

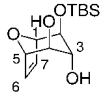
(1*R*,2*R*,4*S*,5*S*)-2-(*tert*-Butyldimethylsilanyloxy)-4-hydroxy-8-oxabicyclo-[3.2.1]oct-6-en-3-one [(+)-13] and





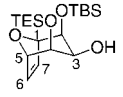
(1*R*,2*R*,4*S*,5*S*)-2-(*tert*-butyldimethylsilanyloxy)-4-triethylsilanyloxy-8-oxabicyclo[3.2.1]oct-6-en-3-one [(−)-14]: *m*CPBA (70%) (274 mg, 1.10 mmol) was added at 0°C to a solution of (−)-**11d** (368 g, 1.00 mmol) in THF/H_2O (1:1, 3 mL). After being stirred vigorously for 10 min the mixture was allowed to reach RT and kept stirring for a further 6 h. After the reaction was completed, the resulting mixture was quenched by adding sat. K_2CO_3 solution. After washing with sat. K_2CO_3 solution the organic layer was extracted (EA), dried (Na_2SO_4) and then the solvent was removed under reduced pressure. Flash chromatography (CH/EA) provided (−)-**14** (116 mg, 30%) as a white solid and (+)-**13** (184 mg, 68%) as the polar product (for the X-ray crystal structure see ref. [34]). The product distribution can vary slightly. Alternatively (+)-**13** was prepared by deprotection of (−)-**14**: Trifluoroacetic acid (0.12 mL, 1.6 mmol) was added at 0°C to a solution of (−)-**14** (306 mg, 0.800 mmol) in THF (7 mL) and H_2O (1.4 mL). After stirring for 1 h at 0°C the ice bath was removed. The reaction was stirred at RT for 2 h. The reaction was quenched by addition of a sat. $NaHCO_3$ solution. After neutralization ($NaHCO_3$) the aqueous layer was extracted (EA). The combined organic layers were dried ($MgSO_4$) and the solvent was removed. Flash chromatography (CH/EA) provided (+)-**13** (168 mg, 78%) as a colourless solid. M.p. 48–50°C; $[\alpha]_D^{20} = +24.4$ ($c = 1$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 6.05$ (ddd, $J = 6.2$, 1.9, 0.6 Hz, 1H; H-6), 6.00 (ddd, $J = 6.2$, 1.8, 0.6 Hz, 1H; H-7), 4.64 (m, 1H; H-5), 4.54 (m, 1H; H-1), 3.54 (m, 1H; H-2), 3.50 (m, 1H; H-4), 1.15 (s, 1H; OH), 0.64 (s, 9H; $SiC(CH_3)_3$), −0.14 (s, 3H; $SiCH_3$), −0.16 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 202.53$ (C_q, C-3), 132.77 (CH, C-6), 132.13 (CH, C-7), 83.74 (CH, C-1), 83.03 (CH, C-5), 77.34 (CH, C-2), 77.23 (CH, C-4), 25.59 (CH_3, $SiC(CH_3)_3$), 18.13 (C_q, $SiC(CH_3)_3$), −4.95 (CH_3, $SiCH_3$), −5.24 (CH_3, $SiCH_3$); IR (KBr): $\tilde{\nu} = 3404$, 2956, 2924, 2908, 2852, 1728, 1468, 1408, 1356, 1340, 1320, 1260, 1164, 1096, 1044, 1004, 952, 864, 836, 812, 780, 744, 708 cm^{-1}; MS (80°C): *m*/*z* (%): 213 (2) $[M - C_4H_9]^+$, 195 (10), 177 (7), 158 (34), 156 (100), 145 (92), 139 (70), 111 (31), 75 (44).

Alternatively (−)-**14** was prepared by protection of (+)-**13**: TES-Cl (2.00 mL, 11.9 mmol) was added at 0°C to a solution of imidazole (820 mg, 11.9 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 10 min, then (+)-**13** (2.14 g 7.95 mmol) was added. After being stirred for 30 min at 0°C the mixture was allowed to reach RT and stirring was continued for 2 h. At this point another portion of TES-Cl (0.5 mL, 3 mmol) was added. After being stirred for 1 h the reaction mixture was quenched by addition of sat. NH_4Cl solution and extracted (EA). The combined organic layers were dried ($MgSO_4$) and the solvent was removed. Flash chromatography (CH/EA) gave (−)-**14** (2.63 g, 87%) as a colourless solid. M.p. 34–35°C; $[\alpha]_D^{20} = -1.8$ ($c = 1$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta =$ 6.24 (s, 2H; H-6, H-7), 4.79 (m, 2H; H-1, H-5), 3.65 (t, $J = 0.9$ Hz, 1H; H-2), 3.63 (t, $J = 0.9$ Hz, 1H; H-4), 0.94 (t, $J =$, 9H; $Si(CH_2CH_3)_3$), 0.90 (s, 9H; $SiC(CH_3)_3$), 0.64 (m, 6H; $Si(CH_2CH_3)_3$), 0.12 (s, 3H; $SiCH_3$), 0.08 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 208.83$ (C_q, C-3), 132.62 (CH, C-6), 132.59 (CH, C-7), 83.42 (CH, C-5), 83.36 (CH, C-1), 75.92 (CH, C-4), 75.71 (CH, C-2), 25.79 (CH_3, $SiC(CH_3)_3$), 18.36 (C_q, $SiC(CH_3)_3$), 6.65 (CH_3, $Si(CH_2CH_3)_3$), 4.60 (CH_2, $Si(CH_2CH_3)_3$), −4.71 (CH_3, $SiCH_3$), −5.09 (CH_3, $SiCH_3$); IR (neat): $\tilde{\nu} = 2956$, 2912, 2876, 1728, 1460, 1412, 1252, 1124, 1104, 1068, 1016, 956, 836, 780, 740 cm^{-1}; MS: *m*/*z* (%): 327 (5) $[M - C_4H_9]^+$, 301 (6), 287 (88), 259 (100), 223 (12), 195 (11), 173 (5), 139 (9), 103 (24), 87 (28), 73 (42).

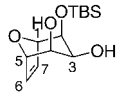


(1*R*,2*S*,3*R*,4*R*,5*S*)-2-(*tert*-Butyldimethylsilanyloxy)-8-oxabicyclo[3.2.1]oct-6-en-3,4-diol [(−)-17]: A solution of (+)-**13** (540 mg, 2.0 mmol) in THF (5 mL) was added at 0°C to a solution of $NaBH(OAc)_3$ (800 mg, 4.0 mmol) in THF (5 mL) and acetic acid (10 mL). After stirring for 2 h at 0°C $NaBH(OAc)_3$ (400 mg, 2.0 mmol) was added. The reaction mixture was stirred for another hour and then quenched by addition of sat. $NaHCO_3$ solution. After neutralization (solid $NaCO_3$) the mixture was extracted (EA) and the combined organic layers were dried (Na_2SO_4). Removal of the solvent and flash chromatography (CH/EA) provided (−)-**17** (480 mg, 87%) as a white solid. M.p. 102°C; $[\alpha]_D^{20} = -0.2$ ($c = 1$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 6.38$ (dd, $J = 6.3$, 1.9 Hz, 1H; H-6), 6.33 (dd, $J = 6.2$, 1.8 Hz, 1H; H-7), 4.73 (m, 1H; H-5), 4.62 (m,

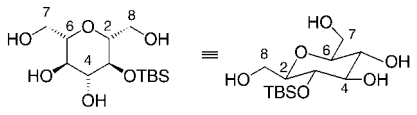
1H; H-1), 3.75 (m, 1H; H-3), 3.49 (m, 1H; H-2), 3.43 (m, 1H; H-4), 1.99 (brs, 1H; 4-OH), 1.89 (d, $J = 9.3$ Hz, 1H; 3-OH), 0.91 (s, 9H; $SiC(CH_3)_3$), 0.11 (s, 6H; $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$): $\delta = 132.62$ (CH, C-6), 132.19 (CH, C-7), 82.92 (CH, C-1), 82.15 (CH, C-5), 77 (CH, C-3), 71.05 (CH, C-2), 70.75 (CH, C-4), 25.71 (CH_3, $SiC(CH_3)_3$), 18.00 (C_q, $SiC(-CH_3)_3$), -4.95 (CH_3, $SiCH_3$); IR ($CHCl_3$): $\tilde{\nu} = 3592$, 3548, 3000, 2956, 2932, 2884, 2856, 1472, 1388, 1360, 1320, 1300, 1260, 1092, 1040, 988, 940; FAB-MS: *m/z* (%): 273 (54) $[M+H]^+$, 259 (12), 215 (20), 187 (9), 176 (8), 167 (9), 154 (18), 136 (23), 129 (22); MS (160 °C): *m/z* (%): 215 (26) $[M - C_4H_9]^+$, 197 (16), 179 (6), 171 (17), 169 (28), 167 (32), 147 (26), 129 (87), 123 (26), 117 (25), 105 (6), 95 (19), 81 (95), 75 (100); HRMS: calcd for $C_9H_{15}O_4Si$: 215.0740, found: 215.0741.



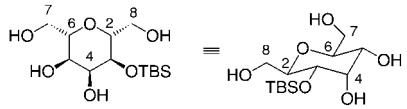
2β-(*tert*-Butyldimethylsilanyloxy)-4β-triethylsilanyloxy-8-oxabicyclo[3.2.1]-oct-6-en-3β-ol [*rac*-14a]: A solution of *rac*-**14** (1.76 g, 4.50 mmol) in MeOH (5 mL) was added at 0 °C to a suspension of $MgBr_2$ (1.65 g, 9.00 mmol) in MeOH (20 mL). $NaBH_4$ was added in small portions until the reaction was complete. After stirring for 1 h the reaction was quenched by addition of sat. NH_4Cl solution. After extraction (EA) the combined organic layers were dried (Na_2SO_4) and the solvent was removed. Flash chromatography (CH/EA) provided *rac*-**14a** (1.73 g, >99%) as a colourless oil. ^1H NMR ($CDCl_3$): $\delta = 6.23$ (s, 2H; H-6, H-7), 4.66 (m, 1H; H-1), 4.64 (m, 1H; H-5), 3.83 (dt, $J = 12.3$, 5.0 Hz, 1H; H-3), 3.69 (m, 2H; H-2, H-4), 2.70 (d, $J = 12.3$ Hz, 1H; OH), 0.99 (t, $J = 7.9$ Hz, 9H; $Si(CH_2CH_3)_3$), 0.93 (s, 9H; $SiC(CH_3)_3$), 0.65 (q, $J = 8.2$ Hz, 6H; $Si(CH_2CH_3)_3$), 0.10 (s, 3H; $SiCH_3$), 0.09 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 132.51$ (CH, C-6), 132. 47 (CH, C-7), 82.69 (CH, C-1), 82.61 (CH, C-5), 68.19 (CH, C-2), 68.01 (CH, C-4), 64.45 (CH, C-3), 25.83 (CH_3, $SiC(CH_3)_3$), 18.21 (C_q, $SiC(CH_3)_3$), 6.81 (CH_3, $Si(CH_2CH_3)_3$), 4.92 (CH_2, $Si(CH_2CH_3)_3$), -4.58 (CH_3, $SiCH_3$), -4.80 (CH_3, $SiCH_3$); IR (neat): $\tilde{\nu} = 3556$, 3080, 2952, 2876, 1460, 1412, 1360, 1312, 1288, 1252, 1132, 1076, 1040, 1004, 972, 944, 892, 860, 836, 776, 740, 708 cm^{-1}; MS: *m/z* (%): 329 (34) $[M - C_4H_9]^+$, 301 (4), 261 (9), 237 (8), 211 (18), 197 (13), 169 (6), 157 (9), 129 (30), 116 (16), 81 (100), 73 (27); HRMS: calcd for $C_{19}H_{38}O_4Si_2$: 386.2309, found: 386.2313.



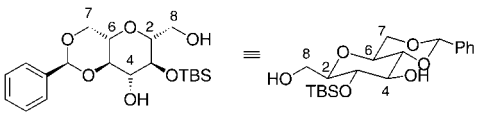
2-(*tert*-Butyldimethylsilanyloxy)-8-oxabicyclo[3.2.1]oct-6-en-3,4-diol (*rac*-18): Trifluoroacetic acid (0.23 mL, 3.00 mmol) was added slowly at 0 °C to a stirred solution of *rac*-**14a** (580 mg, 1.50 mmol) in THF(13 mL) and H_2O (2.5 mL). After 10 min at 0 °C the ice bath was removed and the reaction mixture was stirred for 2.5 h. Addition of $NaHCO_3$ terminated the reaction. The organic layer was neutralized with $NaHCO_3$, extracted (EA) and dried ($MgSO_4$). After removing the solvent flash chromatography provided *rac*-**18** (312 mg, 77%) as a colourless oil. ^1H NMR ($CDCl_3$): $\delta = 6.26$ (dd, $J = 6.3$, 1.6 Hz, 1H; H-6), 6.23 (dd, $J = 6.3$, 1.8 Hz, 1H; H-7), 4.77 (t, $J = 1.9$ Hz, 1H; H-5), 4.63 (t, $J = 1.9$ Hz, 1H; H-1), 3.83 (m, 1H; H-3), 3.76 (m, 1H; H-2), 3.59 (brs, 1H; H-4), 0.93 (s, 9H; $SiC(CH_3)_3$), 0.12 (s, 6H; $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$): $\delta = 132.30$ (CH, C-6), 131.65 (CH, C-7), 82.42 (CH, C-1), 82.21 (CH, C-5), 69.08 (CH, C-3), 68.53 (CH, C-2), 64.57 (CH, C-4), 25.74 (CH_3, $SiC(CH_3)_3$), 18.00 (C_q, $SiC(CH_3)_3$), -4.79 (CH_3, $SiCH_3$), -4.84 (CH_3, $SiCH_3$); IR ($CHCl_3$): $\tilde{\nu} = 3671$, 3530, 2999, 2956, 2931, 2885, 2858, 1617, 1471, 1464, 1416, 1362, 1319, 1304, 1258, 1234, 1126, 1113, 1093, 1067, 1002, 986, 955, 939, 865, 850 cm^{-1}; MS: *m/z* (%): 215 (14) $[M - C_4H_9]^+$, 197 (8), 169 (8), 151 (8), 129 (53), 117 (14), 103 (7), 81 (100), 75 (66).



(2*R*,3*S*,4*R*,5*R*,6*S*)-3-(*tert*-Butyldimethylsilanyloxy)-2,6-bis-hydroxymethyl-4,5-bis-hydroxy-tetrahydropyran [(+)-17a]: Oxabicycle (−)-**17** (470 mg, 1.68 mmol) was dissolved in CH_2Cl_2 (15 mL) and MeOH (2 mL) and the mixture was cooled to −78 °C. Ozone (100 L per h) was bubbled through the reaction flask. When a slight blue colour persisted the ozone was removed by a slight oxygen stream at −78 °C. $NaBH_4$ (166 mg, 4.36 mmol) was added at −78 °C before the cooling bath was removed and the temperature was allowed to reach RT. Stirring was continued for 30 min at RT, and the reaction was quenched by adding 10% citric acid. The mixture was worked up by extraction (EA). The combined organic layers were dried ($MgSO_4$). Removal of the solvent under reduced pressure and purification (CH/EA) afforded (+)-**17a** (513 mg, 99%) as a white solid. M.p. 45 °C; $[\alpha]_D^{20} = +13.9$ ($c = 1$, $CHCl_3$). NMR signals were assigned by 2D techniques: ^1H NMR (CD_3OD): $\delta = 3.76$ (m, 1H; H-2), 3.73 (m, 1H; H-6), 3.50 (dd, $J = 11.5$, 6.2 Hz, 1H; H-7_a), 3.47 (dd, $J = 11.3$, 6.4 Hz, 1H; H-7_b), 3.25 (m, 1H; H- H-8_a), 3.20 (qt, $J = 1.6$ Hz, 1H; H-4), 3.14 (m, 2H; H-5, H-3), 3.07 (dd, $J = 9.4$, 8.6 Hz, 1H; H-8_b), 0.79 (s, 9H; $SiC(CH_3)_3$), 0.05 (s, 3H; $SiCH_3$), 0.00 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 81.02$ (CH, C-2), 80.40 (CH, C-6), 78.00 (CH, C-4), 72.13 (CH, C-3), 71.15 (CH, C-5), 62.30 (CH, C-7), 62.29 (CH, C-8), 25.55 (CH_3, $SiC(CH_3)_3$), 18.13 (C_q, $SiC(CH_3)_3$), -4.34 (CH_3, $SiCH_3$), -5.79 (CH_3, $SiCH_3$); IR (KBr): $\tilde{\nu} = 3384$, 2952, 2928, 2884, 2856, 1472, 1408, 1388, 1360, 1252, 1188, 1132, 1096, 1044, 988, 936, 856, 836, 780 cm^{-1}; MS (150 °C): *m/z* (%): 251 (1) $[M - C_4H_9]^+$, 233 (2), 215 (27), 185 (5), 173 (8), 159 (18), 147 (30), 143 (18), 129 (23), 117 (69), 99 (26), 85 (4), 75 (100); HRMS: calcd for $C_9H_{19}O_6Si$: 251.0950, found: 251.0950.

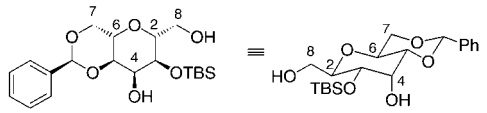


3α-(*tert*-Butyldimethylsilanyloxy)-2β,6β-bis-hydroxymethyl-4α,5α-bis-hydroxy-tetrahydropyran (*rac*-18a): Oxabicycle *rac*-**18** (240 mg, 0.90 mmol) in CH_2Cl_2 (14 mL) and MeOH (2 mL) was allowed to react as described above to afford *rac*-**18a** (271 mg, 98%) after purification (CH/EA) as a white solid. M.p. 46 °C. NMR signals were assigned by 2D techniques: ^1H NMR (CD_3OD): $\delta = 3.92$ (t, $J = 2.5$ Hz, 1H; H-4), 3.74 (m, 1H; H-7_a), 3.70 (dd, $J = 11.4$, 1.9 Hz, 1H; H-8_a), 3.58–3.48 (m, 4H, H-2, H-6, H-5, H-7_b), 3.46 (dd, $J = 11.2$, 5.5 Hz, 1H; H-8_b), 3.32 (dd, $J = 9.4$, 2.6 Hz, 1H; H-3), 0.84 (s, 9H; $SiC(CH_3)_3$), 0.05 (s, 3H; $SiCH_3$), 0.03 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 76.86$ (CH, C-6), 76.71 (CH, C-2), 73.29 (CH, C-4), 70.86 (CH, C-5), 69.31 (CH, C-3), 63.70 (CH_2, C-8), 63.55 (CH_2, C-7), 26.62 (CH_3, $SiC(CH_3)_3$), 19.21 (C_q, $SiC(CH_3)_3$), -3.82 (CH_3, $SiCH_3$), -4.47 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3365$, 2929, 2885, 2857, 1463, 1410, 1360, 1336, 1252, 1092, 1041, 963, 939, 776 cm^{-1}; MS (190 °C): *m/z* (%): 251 (5) $[M - C_4H_9]^+$, 233 (2), 215 (9), 197 (8), 171 (10), 159 (13), 147 (37), 123 (9), 117 (64), 111 (15), 75 (100); HRMS: cald for $C_9H_{19}O_6Si$: 251.0950, found: 251.0951.

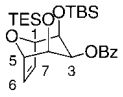


(2*R*,3*S*,4*R*,5*R*,6*S*)-(3-(*tert*-Butyldimethylsilanyloxy)-4-hydroxy-2-hydroxymethyl-(5,6-methyl)-*O*-benzylidene-tetrahydropyran [(+)-25]: Benzaldehyde dimethylacetal (50.0 µl, 0.325 mmol) was added at 0 °C to a solution of (+)-**17a** (98 mg, 0.31 mmol) in CH_2Cl_2 (2 mL). After addition of a catalytic amount of pyridinium toluene-4-sulfonate the reaction mixture was stirred for 48 h at RT. The reaction mixture was poured into sat. $NaHCO_3$ solution and the aqueous layer was extracted (CH_2Cl_2) and dried ($MgSO_4$). After removal of the solvent flash chromatography (CH → CH/EA) afforded (+)-**25** (78 mg, 64%) as a colourless solid. M.p. 97 °C; $[\alpha]_D^{20} = +11.3$ ($c = 1$, $CHCl_3$). NMR signals were assigned by 2D techniques: ^1H NMR (CD_3OD): $\delta = 7.48$ (m, 2H; Ar-H), 7.37 (m, 3H; Ar-H), 5.51 (s, 1H; OC*H*(Ph)O), 4.34 (dd, $J = 10.3$, 4.4 Hz, 1H; H-8_a), 3.88 (dd, $J = 11.8$, 2.6 Hz 1H; H-7_a), 3.72 (m, 1H; H-4), 3.70 (m, 1H; H-7_b), 3.68 (m, 1H; H-8_b), 3.63 (m, 1H; H-5), 3.48 (dt, $J = 9.5$, 4.8 Hz, H-2), 3.42 (m, 2H; H-6, H-3), 0.89 (s, 9H; $SiC(CH_3)_3$), 0.16 (s, 3H; $SiCH_3$), 0.13 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 137.07$ (C_q, Ar-C), 129.23 (CH, Ar-C), 128.33 (CH, Ar-C), 126 (CH,Ar-C), 101.80 (CH, O*C*H(Ph)O), 81.16 (CH, C-3), 80.95 (CH, C-6), 75.42 (CH, C-4), 71.62 (CH, C-5), 70.00 (CH, C-2), 68.80 (CH_2, C-8), 62.14 (CH_2, C-7), 25.90 (CH_3, $SiC(CH_3)_3$), 18.24 (C_q, $SiC(CH_3)_3$), -3.91 (CH_3, $SiCH_3$), -4.98 (CH_3, $SiCH_3$); IR ($CHCl_3$): $\tilde{\nu} = 3602$, 3478, 2957, 2931, 2886, 2858, 1725, 1603, 1471, 1463, 1406, 1387, 1362, 1333, 1315, 1255, 1181, 1099, 1061, 1028, 1008, 988, 976, 916, 872, 855, 839 cm^{-1}; MS (140 °C): *m/z* (%): 396 (1) $[M]^+$, 339 (11), 288 (1), 257 (1), 233 (10), 215 (47), 197 (2), 171 (6), 147 (33), 129 (11), 122 (12), 117 (26), 103 (65), 91 (6), 75 (100).

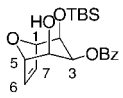
0947-6539/01/0722-4782 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 22



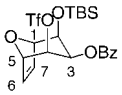
3α-(*tert*-Butyldimethylsilanyloxy)-4α-hydroxy-2β-hydroxymethyl-(5α,6β-methyl)-*O*-benzylidene-tetrahydropyran (*rac*-26): Benzaldehyde dimethylacetal (0.09 mL, 0.6 mmol) was added at 0 °C to a solution of *rac*-**18a** (146 mg, 0.05 mmol) in acetonitrile (1.5 mL). After addition of a catalytic amount of *p*-toluenesulfonic acid the reaction mixture was stirred for 6 h at 65 °C. Another portion of benzaldehyde dimethylacetal (0.05 mL, 0.3 mmol) was added and stirring continued for 12 h at RT. The reaction mixture was worked up by dilution with EA and then a sat. K_2CO_3 solution was added. After stirring for 1 h the organic layer was washed with K_2CO_3 and dried ($MgSO_4$). Removal of the solvent and flash chromatography (CH → CH/EA) afforded *rac*-**26** (69 mg, 36 %) as a colourless solid. M.p. 106 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 7.39$ (m, 2H, Ar-H), 7.22 (m, 3H, Ar-H), 5.48 (s, 1H; OC*H*(Ph)O), 4.18 (dd, $J = 10.2$, 5.3 Hz, 1H; H-7$_a$), 4.09 (t, $J = 2.5$ Hz, 1H; H-4), 3.81 (m, 1H; H-5), 3.7 (dd, $J = 11.4$, 2.0 Hz, 1H; H-8$_a$), 3.68 (m, 1H, H-2), 3.59 (m, 2H; H-7$_b$, H-3), 3.48 (dd, $J = 11.4$, 5.1 Hz, 1H; H-8$_b$), 3.45 (m, 1H; H-6), 0.83 (s, 9H; SiC(CH$_3$)$_3$), 0.05 (s, 3H; SiCH$_3$), 0.03 (s, 3H; SiCH$_3$); ^{13}C NMR (CD_3OD): $\delta = 139.55$ (CH, Ar-C), 130.14 (C$_q$, Ar-C), 129.29 (CH, Ar-C), 127.83 (CH, Ar-C), 103.25 (CH, O*C*H(Ph)O), 80.94 (CH, C-6), 78.24 (CH, C-3), 70.76 (CH, C-4), 70.62 (CH$_2$, C-7), 70.54 (CH, C-2), 66.78 (CH, C-5), 62.94 (CH$_2$, C-8), 26.63 (CH$_3$, SiC(*C*H$_3$)$_3$), 19.23 (C$_q$, Si*C*(CH$_3$)$_3$), −3.76 (CH$_3$, SiCH$_3$), −4.46 (CH$_3$, SiCH$_3$); IR (ATR): $\tilde{\nu} = 3468$, 2929, 2857, 1462, 1388, 1252, 1091, 1038, 1005, 918, 868, 838, 779, 700, 672 cm^{-1}; MS (140 °C): *m*/*z* (%): 396 (2) $[M]^+$, 370 (3), 340 (79), 292 (1), 264 (3), 231 (16), 197 (51), 171 (69), 143 (66), 117 (84), 91 (83), 75 (100); HRMS: calcd for $C_{20}H_{32}O_6Si$: 396.68, found: 396.69.



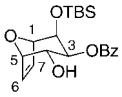
(2β-(*tert*-Butyldimethylsilanyloxy)-4β-triethylsilanyloxy-8-oxa-bicyclo-[3.2.1]oct-6-en-3β-yl) benzoate (*rac*-14b): Benzoyl chloride (44 µl, 0.42 mmol) was added at 0 °C to a solution of equatorial alcohol *rac*-**14a** (110 mg, 0.28 mmol) in acetonitrile (1.4 mL) (Schemes 9, 10). After addition of a catalytic amount of DMAP the reaction mixture was stirred for 12 h at RT and then poured into a mixture of EA and NH_4Cl. The organic layer was washed with brine and dried ($MgSO_4$). After removal of the solvent purification by flash chromatography (EA/CH) afforded *rac*-**14b** (116 mg, 86 %) as a colourless oil. $[\alpha]_D^{20} = -2.7$ ($c = 1$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 8.13$ (m, 2H; *o*-Bz-H), 7.67 (m, 1H; *p*-Bz-H), 7.43 (m, 2H; *m*-Bz-H), 6.35 (s, 2H; H-6, H-7), 5.36 (t, $J = 4.8$ Hz; 1H; H-3), 4.68 (m, 2H; H-1, H-5), 4.01 (m, 2H; H-2, H-4), 0.93 (t, $J = 7.7$ Hz, 9H; Si(CH$_2$*C*H$_3$)$_3$), 0.92 (s, 9H; SiC(CH$_3$)$_3$), 0.60 (q, $J = 7.8$ Hz, 6H; Si(*C*H$_2$CH$_3$)$_3$; 0.02 (s, 3H; SiCH$_3$), −0.07 (s, 3H; SiCH$_3$); ^{13}C NMR ($CDCl_3$): $\delta = 166$ (C$_q$, C=O), 135.0 (CH, C-6), 133.08 (CH, C-7), 132.94 (CH, *p*-Bz-C), 130.55 (CH, *o*-Bz-C), 128.88 (C$_q$, Bz-C), 128.86 (CH, *m*-Bz-C), 83.56 (CH, C-1), 83.43 (CH, C-5), 68.99 (CH, C-3), 66.61 (CH, C-4), 66.49 (CH, C-2), 25.78 (CH$_3$, SiC(*C*H$_3$)$_3$), 18.07 (C$_q$, SiCH$_3$), 6.83 (CH$_3$, Si(CH$_2$CH$_3$)$_3$), 4.98 (CH$_2$, Si(*C*H$_2$CH$_3$)$_3$), −4.68 (CH$_3$, SiCH$_3$), −4.84 (CH$_3$, SiCH$_3$); IR ($CHCl_3$): $\tilde{\nu} = 2958$, 2936, 2911, 2877, 1796, 1711, 1601, 1452, 1366, 1343, 1315, 1281, 1240, 1174, 1148, 1113, 1070, 1040, 1014, 999, 864, 837, 810 cm^{-1}; MS (60 °C): *m*/*z* (%): 433 (1) $[M - C_4H_9]^+$, 226 (4), 198 (3), 179 (2), 129 (1), 105 (100), 86 (24), 78 (21).



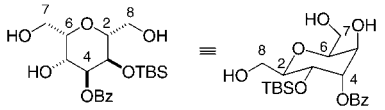
(2β-(*tert*-Butyldimethylsilanyloxy)-4β-hydroxy-8-oxa-bicyclo[3.2.1]oct-6-en-3β-yl) benzoate (*rac*-23): Trifluoroacetic acid (0.28 mL, 3.8 mmol) was added slowly at 0 °C to a stirred solution of *rac*-**14b** (921 mg, 1.90 mmol) in THF (22 mL) and H_2O (3.8 mL). After 10 min the ice bath was removed and the reaction mixture was stirred for 1.5 h at RT. By adding $NaHCO_3$ the reaction was terminated and the organic layer was neutralized (Na_2CO_3). The combined organic layers were extracted (EA) and dried ($MgSO_4$). Removal of the solvent and flash chromatography provided *rac*-**23** (638 mg, 89 %) as a white solid. M.p. 87 °C; ^{1}H NMR ($CDCl_3$): $\delta = 8.12$ (m, 2H; *o*-Bz-H), 7.56 (m, 1H; *p*-Bz-H), 7.43 (m, 2H; *m*-Bz-H), 6.39 (dd, $J = 6.3$, 1.8 Hz, 1H; H-7), 6.35 (dd, $J = 6.3$, 1.8 Hz, 1H; H-6), 5.34 (t, $J = 4.1$ Hz; 1H; H-3), 4.83 (t, $J = 2.0$ Hz, 1H; H-5), 4.68 (t, $J = 2.0$ Hz, 1H; H-1), 4.14 (m, 1H; H-2), 3.87 (m, 1H; H-4), 0.91 (s, 9H; SiC(CH$_3$)$_3$), 0.06 (s, 3H; SiCH$_3$), −0.07 (s, 3H; SiCH$_3$); ^{13}C NMR ($CDCl_3$): $\delta = 166.01$ (C$_q$, C=O), 133.22 (CH,C-6), 133.13 (CH, C-7), 132.21 (CH, *p*-Bz-C), 129.92 (CH, *o*-Bz-C), 128.28 (CH, *m*-Bz-C), 128.19 (C$_q$, Bz-C), 83.11 (CH, C-1), 82.75 (CH, C-5), 68.69 (CH, C-3), 67.49 (CH, C-2), 67.12 (CH, C-4), 25.65 (CH$_3$, SiC(*C*H$_3$)$_3$), 17.83 (C$_q$, Si*C*(CH$_3$)$_3$), −4.84 (CH$_3$, SiCH$_3$), −5.05 (CH$_3$, SiCH$_3$); IR ($CHCl_3$): $\tilde{\nu} = 3534$, 1957, 1932, 1878, 1859, 1712, 1602, 1471, 1452, 1416, 1363, 1341, 1316, 1280, 1261, 1238, 1177, 1122, 1095, 1069, 1006, 959, 858, 840, 818 cm^{-1}; MS (90 °C): *m*/*z* (%): 319 (37) $[M - C_4H_9]^+$, 221 (3), 197 (5), 179 (29), 155 (2), 129 (61), 105 (100), 82 (18), 78 (14), 74 (18).



(2β-(*tert*-Butyldimethylsilanyloxy)-4β-trifluoromethanesulfonyloxy-8-oxa-bicyclo[3.2.1]oct-6-en-3β-yl) benzoate (*rac*-23a): Pyridine (2.7 mL, 27 mmol), DMAP (20 mg, 0.16 mmol) and trifluoromethanesulfonic anhydride (0.275 mL, 1.65 mmol) were added at −1 °C to a solution of *rac*-**23** (412 mg, 1.10 mmol) in CH_2Cl_2 (8 mL). The reaction mixture was stirred for 3 h at −1 °C and worked up by being poured into ice-cold 1N HCl. The organic layer was washed with 1N HCl (3 ×). The combined aqueous layer was reextracted (CH_2Cl_2) and dried ($MgSO_4$). After removal of the solvent flash chromatography (CH → CH/EA) afforded *rac*-**23a** (445 mg, 80 %) as a colourless solid. M.p. 134–136 °C (decomp); ^{1}H NMR ($CDCl_3$): $\delta = 8.14$ (m, 2H; *o*-Bz-H), 7.59 (m, 1H; *p*-Bz-H), 7.45 (m, 2H; *m*-Bz-H), 6.52 (dd, $J = 6.2$, 1.7 Hz, 1H; H-6), 6.38 (dd, $J = 6.4$, 1.8 Hz, 1H; H-7), 5.60 (t, $J = 4.5$ Hz; 1H; H-3), 5.04 (dd, $J = 4.5$, 2.1 Hz, 1H; H-4), 4.99 (t, $J = 1.9$ Hz, 1H; H-5), 4.78 (t, $J = 1.9$ Hz, 1H; H-1), 4.12 (dd, $J = 4.5$, 2.4 Hz, 1H; H-2), 0.90 (s, 9H; SiC(CH$_3$)$_3$), 0.04 (s, 3H; SiCH$_3$), −0.12 (s, 3H; SiCH$_3$); ^{13}C NMR ($CDCl_3$): $\delta = 165.51$ (C$_q$, C=O), 135.41 (CH,C-6), 133.57 (CH, C-7), 131.41 (CH, *p*-Bz-C), 130.11 (CH, *o*-Bz-C), 129.01 (C$_q$, Bz-C), 128.41 (CH, *m*-Bz-C), 116.90 (q, $J = 318.9$ Hz, CF$_3$), 83.58 (CH, C-1), 80.72 (CH, C-5), 79.95 (CH, C-3), 65.98 (CH, C-2), 64.87 (CH, C-4), 25.44 (CH$_3$, SiC(*C*H$_3$)$_3$), 17.85 (C$_q$, Si*C*(CH$_3$)$_3$), −4.68 (CH$_3$, SiCH$_3$), −5.13 (CH$_3$, SiCH$_3$); IR (ATR): $\tilde{\nu} = 3084$, 2962, 2928, 2882, 2855, 1726, 1578, 1587, 1493, 1457, 1401, 1338, 1273, 1250, 1202, 1176, 1145, 1109, 1068, 1013, 978, 939, 900, 870, 845, 832, 816, 783, 719, 700 cm^{-1}; MS (100 °C): *m*/*z* (%): 493 (1) $[M - CH_3]^+$, 451 (100), 423 (1), 359 (3), 319 (3), 291 (1), 237 (2), 179 (26), 136 (12), 129 (10), 105 (82), 81 (11), 77 (11), 73 (12); HRMS: calcd for $C_{21}H_{27}F_3O_7SSi$: 508.1198, found: 508.1200.

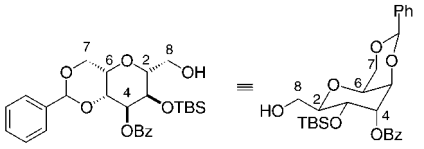


(2β-(*tert*-Butyldimethylsilanyloxy)-4α-hydroxy-8-oxabicyclo[3.2.1]oct-6-en-3β-yl) benzoate (*rac*-24): Tetrabutylammonium nitrite (1.0 g, 3.5 mmol) was added to a solution of triflate *rac*-**23a** (445 mg, 0.875 mmol) in DMF. After complete conversion the reaction was quenched by adding 1N HCl. After 1 h the mixture was extracted (CH_2Cl_2) and dried ($MgSO_4$). Removal of the solvent and flash chromatography (CH/EA) provided *rac*-**24** (228 mg, 76 %) as a colourless solid. M.p. 144–146 °C; ^{1}H NMR ($CDCl_3$): $\delta = 8.06$ (m, 2H; *o*-Bz-H), 7.56 (m, 1H; *p*-Bz-H), 7.43 (m, 2H; *m*-Bz-H), 6.41 (ddd, $J = 6.2$, 1.6, 0.5 Hz, 1H; H-6), 6.36 (dd, $J = 6.2$, 1.8 Hz, 1H; H-7), 5.08 (dd, $J = 8.2$, 4.8 Hz, 1H; H-3), 4.82 (dd, $J = 4.4$, 1.9 Hz, 1H; H-5), 4.66 (t, $J = 1.9$ Hz, 1H; H-1), 4.19 (dd, $J = 8.3$, 4.4 Hz, 1H; H-4), 4.18 (dd, $J = 4.8$, 2.1 Hz, 1H; H-2), 2.2 (br s, 1H; OH), 0.85 (s, 9H; SiC(CH$_3$)$_3$), 0.01 (s, 3H; SiCH$_3$), −0.13 (s, 3H; SiCH$_3$); ^{13}C NMR ($CDCl_3$): $\delta = 166.79$ (C$_q$, C=O), 133.20 (CH, C-6), 132.57 (CH, C-7), 131.78 (CH, *p*-Bz-C), 129.88 (C$_q$, Bz-C), 129.80 (CH, *o*-Bz-C), 128.30 (CH, *m*-Bz-C), 83.59 (CH, C-1), 80.13 (CH, C-5), 76.36 (CH, C-3), 67.47 (CH, C-2), 66.23 (CH, C-4), 25.66 (CH$_3$, SiC(*C*H$_3$)$_3$), 18.00 (C$_q$, Si*C*(CH$_3$)$_3$), −4.77 (CH$_3$, SiCH$_3$), −4.89 (CH$_3$, SiCH$_3$); IR (ATR): $\tilde{\nu} = 3473$, 2951, 2930, 2857, 1688, 1454, 1361, 1346, 1319, 1292, 1248, 1216, 1183, 1132, 1111, 1065, 1027, 988, 909, 884, 862, 836, 808, 775, 714 cm^{-1}; MS (130 °C): *m*/*z* (%): 361 (0.4) $[M - CH_3]^+$, 319 (54), 279 (1), 239 (0.3), 221 (3), 197 (8), 179 (64), 151 (3), 129 (49), 105 (100), 77 (23), 73 (29); calcd for HRMS $C_{20}H_{28}O_5Si$: 376.06, found: 376.07.

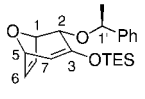


(3α-(*tert*-Butyldimethylsilanyloxy)-2β,6β-bis-hydroxymethyl-5β-hydroxy-tetrahydropyran-4α-yl) benzoate (*rac*-24a): Compound *rac*-**24** (228 mg, 0.600 mmol) in CH_2Cl_2 (5.5 mL) and MeOH (0.75 mL) were allowed to

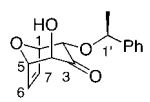
react as described for (+)-**17a**. Purification (MeOH/EA) afforded *rac*-**24a** (115 mg, 47%) as a white solid. M.p. 129°C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 7.94$ (m, 2H; *o*-Bz-H), 7.50 (m, 1H; *p*-Bz-H), 7.38 (m, 2H; *m*-Bz-H), 5.25 (t, $J = 3.5$ Hz, 1H; H-4), 3.99 (dd, $J =$ 9.9, 3.1 Hz, 1H; H-3), 3.73 (m, 4H, H-5, H-8_a, H-6, H-2), 3.65 (dd, $J = 11.3$, 7.7 Hz; 1H; H-7_a), 3.52 (m, 2H; H-7_b, H-8_b), 0.63 (s, 9H; $SiC(CH_3)_3$), −0.01 (s, 3H; $SiCH_3$), −0.02 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 167.28$ (C_q, C=O), 134.74 (CH, *p*-Bz-C), 131.69 (C_q, Bz-C), 130.93 (CH, *o*-Bz-C), 129.94 (CH, *m*-Bz-C), 79.25 (CH, C-2), 77.70 (CH, C-6), 74.61 (CH, C-4), 69.54 (CH, C-5), 66.60 (CH, C-3), 63.79 (CH_2, C-8), 63.22 (CH_2, C-7), 26.38 (CH_3, $SiC(CH_3)_3$), 18.89 (C_q, $SiC(CH_3)_3$), −4.06 (CH_3, $SiCH_3$), −4.64 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3368$, 2930, 2885, 2858, 1722, 1602, 1585, 1452, 1389, 1361, 1315, 1266, 1177, 1102, 1068, 1026, 971, 939, 919, 867, 837, 777, 709 cm^{-1}; MS (160°C): *m*/*z* (%): 355 (30) $[M - C_4H_9]^+$, 337 (4), 233 (11), 215 (17), 197 (9), 179 (74), 143 (20.0), 124 (9), 105 (100), 89 (1), 75 (29).



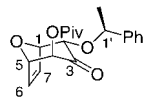
(3*α*-(*tert*-Butyldimethylsilanyloxy)-2*β*-hydroxymethyl-(5*β*-,6*β*-methyl)-*O*-benzylidene-tetrahydropyran-4*α*-yl) benzoate (*rac*-27): Benzaldehyde dimethylacetal (50 µl, 0.34 mmol) was added at 0°C to a solution of *rac*-**24a** (115 mg, 0.280 mmol) in acetonitrile (0.5 mL). After addition of a catalytic amount of *p*-toluenesulfonic acid the reaction mixture was stirred for 3 h at 65°C. After being cooled down to RT the reaction mixture was diluted with EA and after addition of sat. K_2CO_3 solution was stirred for 1 h. The organic layer was washed with sat. K_2CO_3 solution and dried ($MgSO_4$). Removal of the solvent and flash chromatography (CH → CH/EA) afforded *rac*-**27** (55 mg, 39%) as a colourless solid. M.p. 54°C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 7.99$ (m, 2H; *o*-Bz-H), 7.54 (m, 1H; *p*-Bz-H), 7.42 (m, 4H, *m*-Bz-H, *o*-Ph-H), 7.29 (m, 3H; *p*-Ph-H, *m*-Ph-H), 5.57 (s, 1H; OC*H*(Ph)O), 5.37 (t, $J = 3.4$ Hz, 1H; H-4), 4.19 (m, 1H; H-5), 4.17 (dd, $J = 12.6$, 1.0 Hz, 1H; H-7_a), 4.12 (dd, $J = 9.7$, 3.3 Hz, 1H; H-3), 4.05 (dd, $J = 12.6$, 1.8 Hz, 1H; H-7_b), 3.85 (ddd, $J = 9.7$, 5.4, 2.1 Hz, 1H; H-2), 3.79 (dd, $J = 11.8$, 2.1 Hz, 1H; H-8_a), 3.69 (d, $J = 1.2$ Hz, 1H; H-6), 3.61 (dd, $J = 11.8$, 5.4 Hz, 1H; H-8_b), 0.67 (s, 9H; $SiC(CH_3)_3$), 0.01 (s, 3H; $SiCH_3$), 0.00 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 167.18$ (C_q, C=O), 139.62 (C_q, Bz-C), 134.86 (CH, *p*-Bz-C), 131.51 (C_q, Ph-C), 131.04 (CH, *o*-Bz-C), 130.35 (CH, *p*-Ph-C), 129.98 (CH, *m*-Bz-C), 129.49 (CH, *o*-Ph-C), 127.55 (CH, *m*-Ph-C), 102.41 (CH, O*C*H(Ph)O), 78.60 (CH, C-2), 76.44 (CH, C-5), 72.68 (CH, C-4), 70.99 (CH_2, C-7), 68.75 (CH, C-6), 68.34 (CH, C-3), 63.20 (CH_2, C-8), 26.40 (CH_3, $SiC(CH_3)_3$), 18.91 (C_q, $SiC(CH_3)_3$), −4.13 (CH_3, $SiCH_3$), −4.65 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3494$, 2954, 2929, 2857, 1722, 1602, 1585, 1493, 1452, 1401, 1360, 1314, 1266, 1218, 1155, 1102, 1011, 970, 937, 917, 870, 836, 778, 753, 708 cm^{-1}; MS (160°C): *m*/*z* (%): 485 (1) $[M - CH_3]^+$, 443 (49), 379 (2), 337 (30), 321 (8), 291 (1), 261 (2), 215 (23), 197 (10), 179 (88), 155 (5), 129 (7), 117 (12), 105 (100), 77 (16), 75 (12).



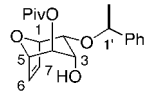
(1′*S*,1*R*,2*S*,5*S*)-2-(1′-Phenylethoxy)-3-triethylsilanyloxy-8-oxabicyclo[3.2.1]-octa-3,6-diene [(−)-12a]: Lithium diisopropylamide (1.3 equiv) [freshly prepared from diisopropylamine (2.66 mL, 18.8 mmol) and *n*BuLi (11.8 mL, 18.8 mmol, 1.6 M solution in hexane)] in THF (11 mL) was added at −78°C to a solution of bicyclic ketone (−)-**12** (3.53 g, 14.5 mmol) and TES-Cl (3.88 mL, 23.1 mmol) in THF (33 mL). After complete addition triethylamine(8.43 mL, 65.1 mmol) was added. The reaction mixture was poured into saturated $NaHCO_3$ solution and extracted (MTBE, 3×). The combined organic layers were dried (Na_2SO_4), concentrated and purified by column chromatography (CH/EA/triethylamine) yielding (−)-**12** (4.85 g, 98%) as a colourless oil. $[\alpha]_D^{20} = -36.0$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 7.38-7.23$ (m, 5H; Ar-H), 6.64 (dd, $J = 6.0$, 1.7 Hz, 1H; H-6), 6.04 (dd, $J = 6.0$, 1.9 Hz, 1H; H-7), 5.29 (d, $J = 4.6$ Hz, 1H; H-4), 4.72 (q, $J = 6.5$ Hz, 1H; H-1′), 4.63 (dd, $J = 4.6$, 1.7 Hz, 1H; H-5), 4.55 (dd, $J = 6.2$, 1.9 Hz, 1H; H-1), 3.97 (d, $J = 6.2$ Hz, 1H; H-2′), 1.41 (d, $J = 6.5$ Hz, 3H; H-2′), 1.01 (t, $J = 7.9$ Hz, 9H; $Si(CH_2CH_3)_3$), 0.71 (q, $J = 7.9$ Hz, 6H; $Si(CH_2CH_3)_3$); ^{13}C NMR ($CDCl_3$): $\delta = 149.46$ (C_q, C-3), 144.39 (C_q, Ar-C), 141.03 (CH, C-7), 128.49 (CH, Ar-CH), 127.53 (CH, Ar-CH), 127.27 (CH, C-6), 126.48 (CH, Ar-CH), 108.42 (CH, C-4), 79.95 (CH, C-5/C-1), 76.49 (CH, C-1′), 73.35 (CH, C-2), 24.06 (CH_3, C-2′), 6.68 (CH_3, $Si(CH_2CH_3)_3$), 5.04 (CH_2, $Si(CH_2CH_3)_3$); IR ($CHCl_3$): $\tilde{\nu} = 3064$, 2960, 2912, 2876, 1636, 1492, 1452, 1412, 1352, 1312, 1280, 1240, 1224, 1088, 1052, 1008, 976, 924, 872, 848, 820 cm^{-1}; MS: *m*/*z* (%): 358 (3) $[M]^+$, 285 (2), 254 (14), 225 (12), 223 (17), 195 (6), 157 (4), 125 (1), 115 (10), 105 (100), 91 (2), 87 (17), 77 (5); HRMS: calcd for $C_{21}H_{30}O_3Si$: 358.1964, found: 358.1965.



(1′*S*,1*R*,2*S*,4*S*,5*S*)-4-Hydroxy-2-(1′-phenylethoxy)-8-oxabicyclo[3.2.1]oct-6-en-3-one [(−)-12b]: *Rubottom-oxidation*:[25] *m*CPBA (70%) (2.93 g, 17.0 mmol) was added at 0°C to a solution of triethylsilyl enol ether (−)-**12a** (5.28 g, 15.5 mmol) in THF/H_2O (1:1, 45.5 mL). After 1 h at 0°C the reaction mixture was stirred at RT for 1.5 h (TLC control), until trifluoroacetic acid (1.18 mL, 15.5 mmol) was added dropwise at 0°C. The cooling bath was removed and the reaction was stirred for a further 4 h at RT. The mixture was washed with 2N aqueous NaOH (2×), the combined aqueous layers were extracted (MTBE, 5×) and dried (Na_2SO_4). Concentration under reduced pressure and purification (CH/EA) yielded (−)-**12b** (3.14 g, 78%) as a white crystalline solid. M.p. 84–86°C; $[\alpha]_D^{20} = -28.3$ ($c = 1.0$, $CHCl_3$). NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.42-7.24$ (m, 5H; Ar-H), 6.48 (ddd, $J = 6.1$, 1.8, 0.6 Hz, 1H; H-7), 6.20 (dd, $J = 6.1$, 1.8 Hz, 1H; H-7), 4.82 (m, 1H; H-5), 4.79 (q, $J = 6.4$ Hz, 1H; H-1′), 4.65 (dd, $J = 5.0$, 1.8 Hz, 1H; H-1), 4.25 (d, $J = 5.0$ Hz, 1H; H-2), 3.78 (d, $J = 1.6$ Hz, 1H; H-4), 2.75 (br s, 1H; OH), 2.23 (d, $J = 6.4$ Hz, 3H; H-2′); ^{13}C NMR ($CDCl_3$): $\delta = 204.79$ (C_q, C-3), 142.98 (C_q, Ar-C), 135.12 (CH, C-7), 130.30 (CH, C-6), 128.64 (CH, Ar-CH), 128.00 (CH, Ar-CH), 126.34 (CH, Ar-CH), 82.90 (CH, C-5), 80.80 (CH, C-2), 80.37 (CH, C-1), 79.19 (CH, C-1′), 76.01 (CH, C-4), 24.02 (CH_3, C-2′), IR ($CHCl_3$): $\tilde{\nu} = 3552$, 3064, 2980, 2932, 2876, 1732, 1600, 1492, 1452, 1376, 1336, 1320, 1280, 1228, 1156, 1108, 1076, 1036, 984, 968, 916, 876, 860, 824 cm^{-1}; MS (60°C): *m*/*z* (%): 258 (1) $[M - 2H]^+$, 240 (1), 225 (1), 164 (1), 156 (3), 150 (6), 138 (10), 106 (13), 105 (100), 91 (4), 81 (2), 77 (6), 69 (5); HRMS: calcd for $C_7H_8O_4$: 156.0422, found: 156.04232.



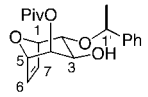
(1′*S*,1*R*,2*S*,4*S*,5*S*)-(2-(1′-Phenylethoxy)-8-oxabicyclo[3.2.1]oct-6-en-3-one-4-yl) pivaloate [(−)-15]: A mixture of hydroxyketone (−)-**12b** (2.47 g, 9.57 mmol), DMAP (152 mg, 1.24 mmol) and triethylamine (1.75 mL, 12.5 mmol) in CH_2Cl_2 (40 mL) was vigorously stirred for 10 min and pivaloyl chloride (1.41 mL) was added dropwise at 0°C. After an additional 10 min at 0°C the cooling bath was removed and the reaction mixture was stirred for 1.5 h at RT. The reaction was terminated by pouring the mixture into sat. $NaHCO_3$ solution. The organic layer was washed with sat. NH_4Cl solution and the combined aqueous layers were extracted (CH_2Cl_2, 3×). Finally the collected organic layers were dried ($MgSO_4$), evaporated in vacuo and purified (CH/EA) to afford (−)-**15** (3.13 g, 95%) as a white crystalline solid. M.p. 98–101°C; $[\alpha]_D^{20} = -31.2$ ($c = 1.0$, $CHCl_3$). NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.40-7.28$ (m, 5H; Ar-H), 6.53 (ddd, $J = 6.1$, 1.6, 0.7 Hz, 1H; H-6), 6.24 (dd, $J = 6.1$, 1.8 Hz, 1H; H-7), 4.89 (m, 1H; H-5), 4.82 (q, $J = 6.5$ Hz, 1H; H-1′), 4.76 (d, $J = 1.1$ Hz, 1H; H-4), 4.66 (dd, $J = 5.0$ Hz, 1.8 Hz, 1H; H-1), 4.15 (d, $J = 5.0$ Hz, 1H; H-2), 1.50 (d, $J =$ 6.5 Hz, 3H; H-2′), 1.17 (s, 9H; $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): $\delta = 202.03$ (C_q, C-3), 177.06 (C_q, C=O), 142.88 (C_q, Ar-C), 135.94 (CH, C-6), 130.49 (CH, C-7), 128.64 (CH, Ar-CH), 128.04 (CH, Ar-CH), 126.40 (CH, Ar-CH), 81.59 (CH, C-2), 80.81 (CH, C-5), 80.24 (CH, C-1), 79.23 (CH, C-1′), 75.28 (CH, C-4), 38.85 (C_q, $C(CH_3)_3$), 26.93 (CH_3, $C(CH_3)_3$), 23.89 (CH_3, C-2′); IR (ATR): $\tilde{\nu} = 2973$, 2968, 2932, 2918, 2874, 1731, 1494, 1479, 1453, 1397, 1369, 1340, 1317, 1307, 1277, 1510, 1133, 1105, 1070, 1032, 1006, 982, 928, 896, 861, 828, 759, 736, 702 cm^{-1}; MS (80°C): *m*/*z* (%): 344 (2) $[M]^+$, 213 (1), 138 (25), 109 (7), 105 (100), 94 (2), 85 (9), 79 (5), 77(5); HRMS: calcd for $C_{20}H_{24}O_5$: 344.1623, found: 344.1618.



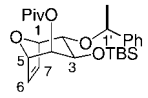
(2*α*-(1′-Phenylethoxy)-3*α*-hydroxy-8-oxabicyclo[3.2.1]oct-6-en-4*β*-yl) pivaloate (*rac*-19): $Ce^{III}Cl_3 \cdot 5H_2O$ (699 mg, 1.88 mmol) was added at −55°C to a solution of ketone *rac*-**15** (646 mg, 1.88 mmol) in THF/EtOH (2:1, 37.5 mL). After 10 min at −55°C $NaBH_4$ (150 mg, 3.44 mmol) was added with vigorous stirring. The temperature was allowed to reach −25°C within 2 h. The reaction mixture was diluted with sat. NH_4Cl solution and extracted (MTBE, 4×). The combined

0947-6539/01/0722-4784 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 22

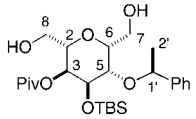
organic layers were dried ($MgSO_4$), the solvent was removed under reduced pressure and the residue was purified by column chromatography (CH/EA) giving *rac*-**19** (584 mg, 90%) as a white solid. M.p. 77.5 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.41-7.28$ (m, 5H; Ar-H), 6.40 (ddd, $J = 6.1$, 1.8, 0.5 Hz, 1H; H-7), 6.25 (dd, $J = 6.1$, 1.6 Hz, 1H; H-6), 4.68 (m, 2H; H-4, H-5), 4.59 (q, $J = 6.4$ Hz, 1H; H-1′), 4.36 (br d, $J = 4.4$ Hz, 1H; H-1), 4.00 (m, 1H; H-3), 3.78 (dd, $J = 5.9$, 4.4 Hz, 1H; H-2), 2.71 (d, $J = 3$Hz, 1H; OH), 1.46 (d, $J = 6.4$ Hz, 3H; H-2′), 1.19 (s, 9H; $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): $\delta = 178.49$ (C_q, C=O), 142.72 (C_q, Ar-C), 133.81 (CH, C-7), 132.22 (CH, C-6), 128.65 (CH, Ar-CH), 128.08 (CH, Ar-CH), 126 (CH, Ar-CH), 80.49 (CH, C-5), 78.64 (CH, C-1), 77.06 (CH, C-1′), 71.47 (CH, C-2), 70.35 (CH, C-4), 68.78 (CH, C-3), 38.85 (C_q, $C(CH_3)_3$), 26.98 (CH_3, $C(CH_3)_3$), 24.10 (CH_3, C-2′); IR ($CHCl_3$): $\tilde{\nu} = 3539$, 3087, 2977, 2932, 2908, 1722, 1602, 1493, 1479, 1454, 1397, 1369, 1338, 1284, 1233, 1159, 1085, 1053, 1034, 1000, 979, 943, 900, 885, 831 cm^{-1}; MS (80 °C): *m*/*z* (%): 346 (0.4) $[M]^+$, 244 (0.3), 226 (1), 215 (2), 181 (4), 139 (55), 112 (5), 111 (68), 106 (10), 105 (100), 103 (23), 93 (5), 85 (11), 83 (12), 81 (10), 79 (6), 77 (5), 69 (4).



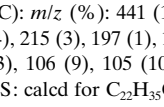
(2*α*-(1′-Phenylethoxy)-3*β*-hydroxy-8-oxabicyclo[3.2.1]oct-6-en-4*β*-yl) pivaloate (*rac*-20): *Triflate inversion*: DMAP (14 mg, 0.028 mmol) and pyridine (0.95 mL) were added successively at −13 °C (ice/NaCl) to a solution of alcohol *rac*-**19**(197 mg, 0.569 mmol) in CH_2Cl_2 (4.75 mL). After 10 min trifluoromethanesulfonic acid anhydride(240 μL, 1.42 mmol) was added by syringe within 15 min. The mixture was stirred for another 50 min at −13 °C. Stirring was continued for 40 min at 0 °C to complete the reaction (TLC control). The dark red mother liquour was used immediately for the next step without further purification or isolation. To the crude triflate solution was added nBu$_4$NNO$_2$ (903 mg, 3.13 mmol) in CH_2Cl_2 (1 mL) dropwise under permanent stirring at −13 °C. The mixture was allowed to slowly reach RT and was stirred for a further 16 h (TLC control) at RT. The mixture was worked up by dilution with CH_2Cl_2 (50 mL) and washed with 1N aqueous HCl (12 mL). The organic layer was separated and the aqueous layer was extracted (CH_2Cl_2, 3×). The organic layers were neutralized (sat. $NaHCO_3$ solution) and dried (Na_2SO_4). After removal of the solvent under reduced pressure purification of the residue (CH/EA) afforded *rac*-**20** (311 mg, 75%) as a white solid. M.p. 93–94 °C. NMR signals were assigned by 2D techniques (additionally the X-ray structure was determined): ^{1}H NMR (CD_2Cl_2): $\delta = 7.39-7.24$ (m, 5H; Ar-H), 6.21 (dd, $J = 6.2$, 1.4 Hz, 1H; H-7), 6.18 (dd, $J = 6.2$, 1.6 Hz, 1H; H-6), 4.89 (dd, $J = 5.3$, 1.8 Hz, 1H; H-4), 4.75 (q, $J = 6.5$ Hz, 1H; H-1′), 4.63 (m, 1H; H-5), 4.32 (dd, $J = 4.3$, 1.4 Hz, 1H; H-1), 3.95 (ddd, $J = 7.8$, 7.6, 5.3 Hz, 1H; H-3), 3.42 (dd, $J = 7.8$, 4.3 Hz, 1H; H-2), 1.98 (d, $J = 7.6$ Hz, 1H; OH), 1.43 (d, $J = 6.5$ Hz, 3H; H-2′), 1.22 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (CD_2Cl_2): $\delta = 178.64$ (C_q, C=O), 145.10 (C_q, Ar-C), 133.79 (CH, C-7), 130.52 (CH, C-6), 128.8.3 (CH, Ar-CH), 127.97 (CH, Ar-CH), 127 (CH, Ar-CH), 80.79 (CH, C-5), 79.46 (CH, C-1′), 79.30 (CH, C-1), 77.20 (CH, C-2), 70.91 (CH, C-3), 69.81 (CH, C-4), 39.40 (C_q, $C(CH_3)_3$, 27.31 (CH_3, $C(CH_3)_3$), 24.40 (CH_3, C-2′); IR (ATR): $\tilde{\nu} = 3437$, 2975, 2931, 2908, 1720, 1492, 1476, 1456, 1395, 1365, 1344, 1322, 1286, 1250, 1229, 1209, 1173, 1111, 1091, 1067, 1028, 992, 944, 903, 860, 830, 762, 735, 700 cm^{-1}; MS (80 °C): *m*/*z* (%): 346 (1) $[M]^+$, 240 (1), 223 (4), 215 (2), 181 (4), 149 (1), 140 (4), 139 (55), 112 (5), 111 (65), 106 (11), 105 (100), 103 (20), 93 (4), 85 (17), 83 (11), 81 (5), 79 (7), 77 (7), 69 (4).



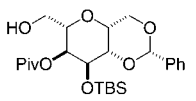
(3*β*-(*tert*-Butyldimethylsilanyloxy)-2*α*-(1′-phenylethoxy)-8-oxabicyclo-[3.2.1]oct-6-en-4*β*-yl) pivaloate [*rac*-20a]: Alcohol *rac*-**20** (916 mg, 2.65 mmol) in DMF (1 mL) was added at 0 °C to a solution of TBS-Cl (998 mg, 6.62 mmol) and imidazole (901 mg, 13.2 mmol) in DMF (1 mL). The ice bath was removed and the reaction mixture was stirred for 24 h at RT. After quenching the reaction with sat. $KHSO_4$ solution (3 mL) the mixture was diluted with water and MTBE. The aqueous layer was extracted (MTBE, 3×) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent and column chromatography (CH/EA) yielded *rac*-**20a** (1.14 g, 93%) as a white solid. M.p. 97 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_2Cl_2): $\delta = 7.38-7.25$ (m, 5H; Ar-H), 6.18 (dd, $J = 6.1$, 1.4 Hz, 1H; H-7), 6.16 (dd, $J = 6.1$, 1.6 Hz, 1H; H-6), 4.84 (dd, $J = 5.1$, 2 Hz, 1H; H-4), 4.62 (q, $J = 6.5$ Hz, 1H; H-1′), 4.51 (m, 1H; H-5), 4.21 (dd, $J = 4.2$, 1.4 Hz, 1H; H-1), 3.97 (dd, $J = 7.7$, 5.1 Hz, 1H; H-3), 3.47 (dd, $J = 7.7$, 4.2 Hz, 1H; H-2), 1.41 (d, $J = 6.5$ Hz, 3H; H-2′), 1.21 (s, 9H; $C(CH_3)_3$), 0.90 (s, 9H; $SiC(CH_3)_3$), 0.11 (s, 3H; $SiCH_3$), 0.04 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_2Cl_2): $\delta = 178.22$ (C_q, C=O), 145.44 (C_q, Ar-C), 133.90 (CH, C-7), 130.68 (CH, C-6), 128.83 (CH, Ar-CH), 128.00 (CH, Ar-CH), 126.70 (CH, Ar-CH), 81.00 (CH, C-5), 79.43 (CH, C-1), 79.41 (CH, C-1′), 76.81 (CH, C-2), 70.81 (CH, C-3), 69.73 (CH, C-4), 39.22 (C_q, $C(CH_3)_3$), 27.39 (CH_3, $C(CH_3)_3$), 26.07 (CH_3, $SiC(CH_3)_3$), 24.23 (CH_3, C-2′), 18.26 (C_q, $SiC(CH_3)_3$), −4.28 (CH_3, $SiCH_3$), −4.61 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3033$, 2972, 2930, 2856, 1723, 1493, 1477, 1454, 1394, 1388, 1348, 1283, 1249, 1223, 1207, 1164, 1110, 1087, 1063, 1029, 998, 970, 946, 928, 906, 880, 841, 788, 761, 721, 703 cm^{-1}; MS (70 °C): *m*/*z* (%): 460 (1) $[M]^+$, 404 (11), 329 (1), 299 (7), 253 (16), 226 (11), 225 (58), 197 (3), 187 (1), 169 (1), 149 (26), 129 (6), 117 (3), 115 (6), 106 (12), 105 (100), 97 (2), 85 (7), 83 (27), 77 (5), 73 (21); HRMS: calcd for $C_{26}H_{40}O_5Si$: 460.2645, found: 460.2644.



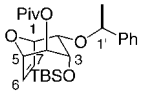
4*α*-(*tert*-Butyldimethylsilanyloxy)-2*β*,6*β*-bis-hydroxymethyl-5*β*-(1′-phenylethoxy)-tetrahydropyran-3*α*-yl) pivaloate (*rac*-20b): Alkene *rac*-**20a** (560 mg, 1.22 mmol) in CH_2Cl_2 (15 mL) and MeOH (1.5 mL) was allowed to react as described for compound (+)-**17a** to afford after chromatography *rac*-**20b** (543 mg, 90%) as a white solid. M.p. 53 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 7.39-7.27$ (m, 5H; Ar-H), 4.96 (dd, $J = 10.3$ Hz, $J = 2.5$ Hz, 1H; H-3), 4.67 (q, $J = 6.4$ Hz, 1H; H-1′), 4.48 (dd, $J = 2.8$, 2.5 Hz, 1H; H-4), 3.93 (ddd, $J = 10.5$ Hz, 6.9, 2.1 Hz, 1H; H-2), 3.84 (ddd, $J = 8.5$, 3.0, 1.5 Hz, 1H; H-6), 3.76 (dd, $J = 11.5$ Hz, $J = 8.5$ Hz, 1H; H-7$_a$), 3.66 (dd, $J = 11.8$, 2.1 Hz, 1H; H-8$_a$), 3.54 (dd, $J = 11.8$, 6.9 Hz, 1H; H-8$_b$), 3.25–3.19 (m, 2H; H-5, H-7$_b$), 1.45 (d, $J = 6.4$ Hz, 3H; H-2′), 1.24 (s, 9H; $C(CH_3)_3$), 0.86 (s, 9H; $SiC(CH_3)_3$), 0.04 (s, 3H; $SiCH_3$), −0.14 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 178.45$ (C_q, C=O), 142.76 (C_q, Ar-C), 128.67 (CH, Ar-CH), 128.19 (CH, Ar-CH), 126.90 (CH, Ar-CH), 76.42 (CH, C-1′), 75.50 (CH, C-6), 75.15 (CH, C-5), 74.13 (CH, C-2), 70.03 (CH, C-3), 66.20 (CH, C-4), 62.82 (CH_2, C-7), 62.35 (CH_2, C-8), 39.01 (C_q, $C(CH_3)_3$), 26.74 (CH_3, $C(CH_3)_3$), 25.24 (CH_3, $SiC(CH_3)_3$), 23.58 (CH_3, C-2′), 17.75 (C_q, $SiC(CH_3)_3$), −5.12 (CH_3, $SiCH_3$), −5.60 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3391$, 2956, 2931, 2884, 2858, 1726, 1467, 1396, 1382, 1282, 1252, 1209, 1152, 1099, 1066, 1047, 1008, 995, 958, 939, 877, 834, 768, 701 cm^{-1}; MS (130 °C): *m*/*z* (%): 441 (1), 440 (3), 439 (8) $[M - C_4H_9]^+$, 336 (2), 335 (7), 233 (4), 215 (3), 197 (1), 185 (2), 177 (1), 160 (2), 159 (14), 143 (4), 141 (2), 117 (3), 106 (9), 105 (100), 85 (3), 79 (2), 77 (2), 75 (7), 73 (9), 69 (2); HRMS: calcd for $C_{22}H_{35}O_7Si$: 439.2152, found: 439.2153.



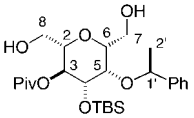
4*α*-(*tert*-Butyldimethylsilanoxy)-2*β*,6*β*-bis-hydroxymethyl-5*β*-hydroxy-tetrahydropyran-3*α*-yl) pivaloate (*rac*-20c): Pearlman-catalyst ($Pd(OH)_2$/C, 20% Pd, 50% moisture) (122 mg) was added under N_2 to a solution of diol *rac*-**20b** (402 mg, 0.810 mmol) in EtOH (8.5 mL). The reaction mixture was flushed several times with hydrogen and stirred at RT under a stable hydrogen atmosphere for 16 h. After complete reaction (TLC control) the mixture was filtered, evaporated under reduced pressure and purified by column chromatography (CH/EA) giving *rac*-**20c** (295 mg, 93%) as a white solid. M.p. 133 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 4.98$ (dd, $J = 10.3$ Hz, 2.8 Hz, 1H; H-3), 4.16 (dd, $J = 3.9$, 2.8 Hz, 1H; H-4), 3.94–3.88 (m, 2H; H-2, H-6), 3.75 (dd, $J = 11.6$, 7.7 Hz, 1H; H-7$_a$), 3.66 (dd, $J = 4.1$, 1.1 Hz, 1H; H-5), 3.64–3.58 (m, 2H; H-7$_a$, H-8$_a$, 3.53 (dd, $J = 11.8$, 6.7 Hz, 1H; H-8$_b$), 1.21 (s, 9H; $C(CH_3)_3$), 0.95 (s, 9H; $SiC(CH_3)_3$), 0.10 (s, 3H; $SiCH_3$), 0.08 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 179.23$ (C_q, C=O), 76.42 (CH, C-6), 75.49 (CH, C-2), 71.93 (CH, C-5), 71.50 (CH, C-4), 70.16 (CH, C-3), 63.31 (CH_2, C-8), 63.11 (CH_2, C-7), 39.96 (C_q, $C(CH_3)_3$), 27.73 (CH_3, $C(CH_3)_3$), 26.34 (CH_3, $SiC(CH_3)_3$), 18.84 (C_q, $SiC(CH_3)_3$), −4.13 (CH_3, $SiCH_3$), −4.58 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3370$, 2955, 2929, 2885, 2857, 1730, 1472, 1462, 1397, 1362, 1282, 1253, 1151, 1098, 1040, 992, 954, 879, 861, 835, 776 cm^{-1}; MS (130 °C): *m*/*z* (%): 337 (4), 336 (11), 335 (52) $[M - C_4H_9]^+$, 317 (3), 259 (7), 233 (18), 216 (3), 215 (22), 197 (13), 189 (2), 187 (5), 185 (22), 173 (8), 171 (7), 167 (2), 160 (13), 159 (100), 155 (11), 147 (7), 143 (20), 141 (17), 131 (14), 129 (23), 123 (10), 117 (23), 111 (8), 95 (5), 85 (19), 81 (11), 77 (5), 75 (48), 73 (47), 69 (11); HRMS: calcd for $C_{14}H_{27}O_7Si$: 335.1526, found: 335.1526.



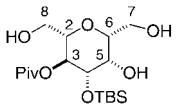
(4α-(*tert*-Butyldimethylsilanyloxy)-2β-hydroxymethyl-(5β,6β-methyl)-*O*-benzylidene-tetrahydropyran-3α-yl) pivaloate (*rac*-28): *p*-Toluenesulfonic acid (2.0 mg, 0.012 mmol) was added to the triol ***rac*-20c** (168 mg, 0.428 mmol) in acetonitrile (2 mL) and the reaction mixture was heated to 65 °C. Benzaldehyde dimethylacetal (80 µl, 0.6 mmol) was added dropwise in three portions at 65 °C. The reaction flask was flushed several times with N_2 and progress of the reaction while the reaction was monitored by TLC. Addition of sat. K_2CO_3 solution (5 mL) terminated the reaction after 2 h. The mixture was stirred vigorously stirring for 15 min, diluted with MTBE and further sat. K_2CO_3 solution. The aqueous layer was extracted (MTBE, 5 ×) and the combined organic layers were dried (Na_2SO_4). Evaporation of the solvent afforded an oily residue which was purified by chromatography (CH/EA) giving *rac*-**28** (176 mg, 85 %) as a white solid. M.p. 134 – 135 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 7.44 - 7.39$ (m, 2H; *m*-Ar-H), 7.30 – 7.24 (m, 3H; *o*-/*p*-Ar-H), 5.55 (s, 1H; CHPh), 5.00 (dd, $J =$ 10.2 Hz, $J = 2.6$ Hz, 1H; H-3), 4.23 (br dd, $J = 2.6$, 1.0 Hz, 1H; H-4), 4.13 (dd, $J = 12.4$, 1.2 Hz, 1H; H-7$_a$), 4.03 (dd, $J = 12.4$, 1.6 Hz, 1H; H-7$_b$), 3.98 – 3.92 (m, 2H; H-2, H-6), 3.67 (br d, $J = 1.0$ Hz, 1H; H-5), 3.60 (dd, $J = 12.2$, 2.0 Hz, 1H; H-8$_a$), 3.50 (dd, $J = 12.2$, 5.3 Hz, 1H; H-8$_b$), 1.13 (s, 9H; $C(CH_3)_3$), 0.87 (s, 9H; $SiC(CH_3)_3$), 0.06 (s, 3H; $SiCH_3$), 0.01 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 179.27$ (C_q, C=O), 139.40 (C_q, Ar-C), 129.98 (CH, *p*-Ar-CH), 129.11 (CH, *o*-Ar-CH), 127.38 (CH, *m*-Ar-CH), 101.93 (CH, CHPh), 78.69 (CH, C-6), 74.75 (CH, C-2), 70.89 (CH, C-7), 70.10 (CH, C-3), 69.56 (CH, C-4), 67.68, (CH_2, C-5), 62.87 (CH_2, C-8), 39.97 (C_q, $C(CH_3)_3$), 27.73 (CH_3, $C(CH_3)_3$), 26.32 (CH_3, $SiC(CH_3)_3$), 18.87 (C_q, $SiC(CH_3)_3$), −4.17 (CH_3, $SiCH_3$), −4.70 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} =$ 3415, 2957, 2928, 2884, 2856, 1721, 1472, 1458, 1404, 1362, 1284, 1252, 1216, 1153, 1105, 1078, 1045, 996, 966, 940, 926, 908, 887, 862, 832, 816, 777, 758, 728, 698 cm^{-1}; MS (150 °C): *m*/*z* (%): 480 (1) $[M]^+$, 424 (12), 423 (42), 347 (7), 321 (13), 281 (3), 269 (4), 233 (4), 216 (8), 215 (52), 197 (26), 185 (25), 171 (11), 169 (9), 160 (17), 159 (100), 155 (14), 149 (16), 143 (16), 141 (20), 136 (16), 131 (15), 129 (19), 123 (20), 117 (20), 111 (13), 108 (13), 105 (33), 91 (21), 85 (27), 75 (50), 73 (60), 69 (12); HRMS: calcd for $C_{25}H_{40}O_7Si$: 480.2543, found: 480.2538.



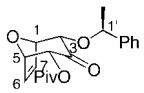
(3α-(*tert*-Butyldimethylsilanyloxy)-2α-(1′-phenylethoxy)-8-oxabicyclo-[3.2.1]oct-6-en-4β-yl) pivaloate (*rac*-19a): Alcohol *rac*-**19** (310 mg, 0.896 mmol), TBS-Cl (270 mg, 1.79 mmol), imidazole (244 mg, 3.58 mmol) and a catalytic amount of DMAP were allowed to react for 36 h (as described for compound *rac*-**20a**) to afford after chromatography (CH/EA) *rac*-**19a** (399 mg, 95 %) as a colourless oil. NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.35 - 7.22$ (m, 5H; Ar-H), 6.28 (ddd, $J = 6.1$, 1.8, 0.8 Hz, 1H; H-7), 6.02 (ddd, $J = 6.1$, 1.8, 0.5 Hz, 1H; H-6), 4.56 (m, 1H; H-5), 4.49 (q, $J = 6.4$ Hz, 1H; H-1′), 4.48 (t, $J = 1.8$ Hz, 1H; H-4), 4.22 (m, 1H; H-1), 3.96 (m, 1H; H-3), 3.69 (dd, $J = 4.9$, 3.9 Hz, 1H; H-2), 1.41 (d, $J = 6.4$ Hz, 3H; H-2′), 1.18 (s, 9H; $C(CH_3)_3$), 0.92 (s, 9H; $SiC(CH_3)_3$), 0.12 (s, 3H; $SiCH_3$), 0.11 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 177.69$ (C_q, C=O), 144.39 (C_q, Ar-C), 135.06 (CH, C-7), 129.82 (CH, C-6), 128.49 (CH, Ar-CH), 127.67 (CH, Ar-CH), 126 (CH, Ar-CH), 80.22 (CH, C-5), 79.36 (CH, C-1), 77.37 (CH, C-1′), 74.72 (CH, C-2), 72.60 (CH, C-4), 70.34 (CH, C-3), 38.73 (C_q, $C(CH_3)_3$), 27.04 (CH_3, $C(CH_3)_3$), 25.75 (CH_3, $SiC(CH_3)_3$), 24.44 (CH_3, C-2′), 18.03 (C_q, $SiC(CH_3)_3$), −4.75 (CH_3, $SiCH_3$), −5.04 (CH_3, $SiCH_3$); IR ($CHCl_3$): $\tilde{\nu} = 3086$, 2956, 2930, 2886, 2857, 1720, 1602, 1472, 1465, 1397, 1371, 1318, 1302, 1284, 1253, 1155, 1129, 1102, 1087, 1070, 1033, 1006, 980, 964, 940, 916, 898, 874, 857, 839 cm^{-1}; MS (90 °C): *m*/*z* (%): 404 (5), 403 (17) $[M - C_4H_9]^+$, 329 (1), 299 (23), 253 (9), 226 (15), 225 (81), 189 (7), 167 (3), 159 (4), 148 (4), 147 (25), 129 (2), 117 (5), 115 (8), 106 (9), 105 (100), 85 (7), 81 (30), 77 (2), 75 (6), 73 (25); HRMS: calcd for $C_{22}H_{31}O_5Si$: 403.1940, found: 403.1941.



(4β-(*tert*-Butyldimethylsilanyloxy)-2β,6β-bis-hydroxymethyl-5β-(1′-phenylethoxy)-tetrahydropyran-3α-yl) pivaloate (*rac*-19b): Alkene *rac*-**19a** (316 mg, 0.687 mmol) in CH_2Cl_2 (8.3 mL) and MeOH (0.83 mL) were allowed to react as described for compound (+)-**17** to afford after chromatography (CH/EA) *rac*-**19b** (313 mg, 91 %) as a white solid. M.p. 148 °C; ^{1}H NMR ($CDCl_3$): $\delta =$ 7.39 – 7.27 (m, 5H; Ar-H), 5.30 (t, $J = 9.5$ Hz, 1H; H-3), 4.89 (q, $J =$ 6.5 Hz, 1H; H-1′), 3.84 (dd, $J = 9.5$, 2.5 Hz, 1H; H-4), 3.84 (br d, $J =$ 2.5 Hz, 1H; H-5), 3.75 – 3.50 (m, 3H; H-2, H-8$_a$, H-8$_b$), 3.38 – 3.30 (m, 2H; H-6, H-7$_a$), 3.02 (dd, $J = 11.5$, 4.9 Hz, 1H; H-7$_b$), 1.52 (d, $J = 6.5$ Hz, 3H; H-2′), 1.23 (s, 9H; $C(CH_3)_3$), 0.96 (s, 9H; $SiC(CH_3)_3$), 0.22 (s, 3H; $SiCH_3$), 0.14 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 178.15$ (C_q, C=O), 143.24 (C_q, Ar-C), 128.57 (CH, Ar-CH), 128.07 (CH, Ar-CH), 126.88 (CH, Ar-CH), 79.19 (CH, C-2), 79.03 (CH, C-6), 78.54 (CH, C-1′), 75.22 (CH, C-3), 74.98 (CH, C-5), 69.77 (CH, C-4), 62.17 (CH_2, C-8), 62.10 (CH_2, C-7), 39.01 (C_q, $C(CH_3)_3$), 27.49 (CH_3, $C(CH_3)_3$), 25.77 (CH_3, $SiC(CH_3)_3$), 23.37 (CH_3, C-2′), 17.85 (C_q, $SiC(CH_3)_3$), −3.09 (CH_3, $SiCH_3$), −4.99 (CH_3, $SiCH_3$); IR ($CHCl_3$): $\tilde{\nu} = 3679$, 3589, 2960, 2932, 2884, 2860, 1730, 1602, 1479, 1462, 1397, 1371, 1277, 1256, 1158, 1137, 1101, 1081, 1068, 1039, 948, 885, 862, 839 cm^{-1}; MS (120 °C): *m*/*z* (%): 496 (3) $[M]^+$, 440 (4), 439 (11), 336 (7), 335 (22), 317 (4), 233 (5), 215 (5), 197 (4), 185 (4), 177 (3), 160 (4), 159 (16), 143 (6), 141 (6), 117 (3), 106 (11), 105 (100), 96 (3), 85 (4), 82 (4), 76 (7), 74 (8), 70 (5); HRMS: calcd for $C_{26}H_{24}O_7Si$: 496.2856, found: 496.2854.

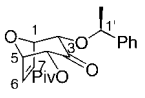


(4β-(*tert*-Butyldimethylsilanyloxy)-2β,6β-bis-hydroxymethyl-5β-hydroxy-tetrahydropyran-3α-yl) pivaloate (*rac*-29): Diol *rac*-**19b** (149 mg, 0.300 mmol) and Pearlman's catalyst (45 mg) were allowed to react as described for compound *rac*-**20c** to afford after chromatography (CH/EA) *rac*-**29**(156 mg, 94 %) as a white solid. M.p. 150 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 5.05$ (t, $J = 9.5$ Hz, 1H; H-3), 3.91 (dd, $J = 9.5$, 3.4 Hz, 1H; H-4), 3.86 (dd, $J = 3.4$, 0.7 Hz, 1H; H-5), 3.79 (dd, $J = 11.4$, 7.7 Hz, 1H; H-7$_a$), 3.64 (dd, $J = 11.4$ Hz, 4.4 Hz, 1H; H-7$_b$), 3.55 (ddd, $J = 7.7$, 4.4, 0.7 Hz, 1H; H-6), 3.52 – 3.46 (m, 2H; H-8$_a$, H-8$_b$), 3.45 – 3.38 (m, 1H; H-2), 1.22 (s, 9H; $C(CH_3)_3$), 0.89 (s, 9H; $SiC(CH_3)_3$), 0.15 (s, 3H; $SiCH_3$), 0.10 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 179.10$ (C_q, C=O), 80.30 (CH, C-6), 80.12 (CH, C-2), 75.37 (CH, C-4), 71.35 (CH, C-5), 71.03 (CH, C-3), 63.16 (CH_2, C-8), 63.04 (CH_2, C-7), 39.90 (C_q, $C(CH_3)_3$), 27.80 (CH_3, $C(CH_3)_3$), 26.37 (CH_3, $SiC(CH_3)_3$), 18.85 (C_q, $SiC(CH_3)_3$), −3.75 (CH_3, $SiCH_3$), −4.53 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3239$, 2930, 2856, 1735, 1475, 1461, 1383, 1362, 1329, 1281, 1248, 1143, 1112, 1068, 1050, 1006, 989, 956, 924, 886, 862, 836, 777 cm^{-1}; MS (160): *m*/*z* (%): 335 (52) $[M - C_4H_9]^+$, 317 (16), 259 (3), 233 (10), 216 (3), 215 (20), 197 (43), 189 (12), 186 (47), 173 (27), 171 (17), 167 (11), 160 (18), 159 (100), 155 (13), 147 (12), 143 (27), 141 (43), 131 (17), 129 (28), 123 (36), 117 (40), 111 (29), 95 (11), 85 (16), 81 (25), 77 (8), 75 (77), 73 (50), 69 (17); HRMS: calcd for $C_{14}H_{27}O_7Si$: 335.1526, found: 335.1526.

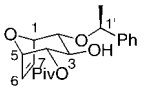


(1′*S*,1*R*,2*S*,4*R*,5*S*)-(2-(1′-Phenylethoxy)-8-oxabicyclo[3.2.1]octa-6-ene-3-one-4-yl) pivaloate [(−)-16]: Ketone (−)-**15** (2.40 g, 6.97 mmol) was dissolved in acetonitrile (24 mL) under ultrasonication within 10 min. DBU(2.08 mL, 14.0 mmol) was added to this solution and the reaction mixture (TLC control) was ultrasonicated for 100 min at 16 – 18 °C. After complete reaction the mixture was poured into sat. NH_4Cl solution and extracted (MTBE, 4 ×). The combined organic layers were dried ($MgSO_4$), concentrated and purified by column chromatography (CH/EA) to afford crystalline (−)-**16** (2.04 g, 85 %). M.p. 130 – 132 °C; $[\alpha]_D^{20} = -58.1$ ($c = 1.0$, $CHCl_3$). NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.40 - 7.27$ (m, 5H; Ar-H), 6.46 (dd, $J = 6.1$, 1.6 Hz, 1H; H-6), 6.32 (dd, $J = 6.1$, 1.8 Hz, 1H; H-7), 5.30 (d, $J = 5.0$ Hz, 1H; H-4), 5.02 (dd, $J = 5.0$, 1.6 Hz, 1H; H-5), 4.76 (q, $J = 6.5$ Hz, 1H; H-1′), 4.74 (dd, $J = 5.3$, 1.8 Hz, 1H; H-1), 4.04 (d, $J = 5.3$ Hz, 1H; H-2), 1.48 (d, $J = 6.5$ Hz, 3H; H-2′), 1.26 (s, 9H; $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): $\delta = 200.35$ (C_q, C-3), 177.08 (C_q, CO_2), 142.87 (C_q, Ar-C), 134.06 (CH, C-6), 132.25 (CH, C-7), 128.67 (CH, Ar-CH), 128.01 (CH, Ar-CH), 126.33 (CH, Ar-CH), 81.40 (CH, C-2), 80.02 (CH, C-5), 79.41 (CH, C-1), 79.01 (CH, C-1′), 76.24 (CH, C-4), 38.85 (C_q, $C(CH_3)_3$), 27.14 (CH_3, $C(CH_3)_3$), 24.07 (CH_3, C-2′); IR (ATR): $\tilde{\nu} = 2973$, 2930, 2917, 1741, 1728, 1482, 1454, 1398, 1372, 1341, 1286, 1273, 1231, 1208, 1145, 1097, 1076, 1054, 1028, 1009, 997, 982, 941, 905, 866, 836, 806, 759, 738, 702 cm^{-1}; MS (110 °C): *m*/*z* (%): 344 (0.4) $[M]^+$, 239 (1), 213 (2), 185 (1), 145 (1), 138 (50), 122 (1), 109 (13), 106 (15), 105 (100), 91 (1), 85 (14), 79 (8), 77 (8), 69 (2); HRMS: calcd for $C_{20}H_{24}O_5$: 344.1623, found: 344.1619.

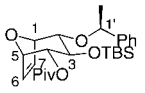
0947-6539/01/0722-4786 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 22



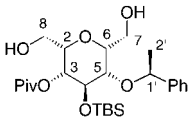
(1′*S*,1*R*,2*R*,3*S*,4*S*,5*S*)-(3-Hydroxy-2-(1′-phenylethoxy)-8-oxabicyclo[3.2.1]-oct-6-en-4-yl) pivaloate [(−)-21]: $Ce^{III}Cl_3 \cdot 5H_2O$ (1.39 g, 3.74 mmol) was added at 0 °C to a solution of ketone (−)-**16** (1.29 g, 3.74 mmol) in THF/EtOH (2:1, 75 mL). After 10 min at 0 °C, $NaBH_4$ (424 mg, 11.2 mmol) was added under vigorous stirring. The temperature was allowed to reach 11 °C within 3 h, then the mixture was worked up as described for *rac*-**19**. Column chromatography (CH/EA) yielded (−)-**21** (1.28 g, 99 %) as a white solid. M.p. 90–91 °C; $[\alpha]_D^{20} = -50.5$ ($c = 1.0$, $CHCl_3$). NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.27-7.24$ (m, 5H; Ar-H), 6.44 (dd, $J = 6.3$, 1.6 Hz, 1H; H-7), 6.40 (dd, $J = 6.3$, 1.5 Hz, 1H; H-6), 4.73 (dd, $J = 5.0$ Hz, 4.6 Hz, 1H; H-4), 4.60 (q, $J = 6.4$ Hz, 1H; H-1′), 4.59–4.54 (m, 2H; H-3, H-5), 4.42 (m, 1H; H-1), 3.62 (dd, $J = 5.1$, 4.4 Hz, 1H; H-2), 2.31 (br s, 1H; OH), 1.43 (d, $J = 6.4$ Hz, 5H; H-2′), 1.24 (s, 9H; $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): $\delta = 177.52$ (C_q, C=O), 142.72 (C_q, Ar-C), 134.10 (CH, C-7), 133.96 (CH, C-6), 128.65 (CH, Ar-CH), 128.00 (CH, Ar-CH), 128.20 (CH, Ar-CH), 79.42 (CH, C-1), 78.39 (CH, C-5), 76.09 (CH, C-1′), 70.70 (C-2), 68.37 (CH, C-4), 65.43 (CH, C-3), 38.85 (C_q, $C(CH_3)_3$), 27.14 (CH_3, $C(CH_3)_3$), 24.24 (CH_3, C-2′); IR (ATR): $\tilde{\nu} = 3539$, 3089, 2968, 2943, 2904, 2878, 1723, 1479, 1454, 1396, 1354, 1285, 1169, 1102, 1073, 1055, 1038, 1007, 968, 954, 887, 859, 839, 808, 762, 742, 699 cm^{-1}; MS (90 °C): *m*/*z* (%): 346 (1) $[M]^+$, 226 (4), 215 (2), 181 (3), 149 (2), 140 (5), 139 (42), 112 (5), 111 (72), 106 (9), 105 (100), 103 (15), 94 (5), 85 (9), 83 (17), 81 (9), 79 (9), 77 (8), 69 (5).



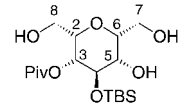
(1′*S*,1*R*,2*R*,3*R*,4*S*,5*S*)-(3-Hydroxy-2-(1′-phenylethoxy)-8-oxabicyclo[3.2.1]oct-6-en-4-yl) pivaloate [(−)-22]: *Triflate inversion*: Alcohol (−)-**21** (520 mg, 1.50 mmol), DMAP (37 mg, 0.30 mmol), pyridine (3.75 mL) and trifluoromethanesulfonic acid anhydride (646 µl, 3.76 mmol) were allowed to react as described for compound *rac*-**20** for 2 h at 0 °C and 1 h at 40 °C. A solution of the crude triflate in DMSO (7 mL) was treated with nBu_4NONO (2.17 g, 7.51 mmol) at 0 °C. After 16 h at RT the mixture was worked up as described for *rac*-**20** to afford after purification (CH/EA) (−)-**22** (311 mg, 60 %) as a colourless crystals. M.p. 110 °C; $[\alpha]_D^{20} = -14.8$ ($c = 0.5$, $CHCl_3$). NMR signals were assigned by 2D techniques (additonally the X-ray structure was determined): ^{1}H NMR (CD_3OD): $\delta = 7.41-7.25$ (m, 5H; Ar-H), 6.23 (dd, $J = 6.3$, 1.8 Hz, 1H; H-7), 6.14 (br dd, $J = 6.3$, 1 Hz, 1H; H-6), 4.77 (q, $J = 6.5$ Hz, 1H; H-1′), 4.61–4.56 (m, 2H; H-4, H-5), 4.19 (dd, $J = 4.4$, 1.8 Hz, 1H; H-1), 3.66–3.59 (m, 1H; H-3), 3.34 (dd, $J = 7.4$, 4.4 Hz, 1H; H-2), 1.42 (d, $J = 6.4$ Hz, 5H; H-2′), 1.20 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (CD_3OD): $\delta = 179.49$ (C_q, C=O), 145.88 (C_q, Ar-C), 133.24 (CH, C-7), 130.89 (CH, C-6), 129.58 (CH, Ar-CH), 128.81 (CH, Ar-CH), 127.46 (CH, Ar-CH), 80.84 (CH, C-1), 80.67 (CH, C-1′), 79.30 (CH, C-2), 78.99 (CH, C-4), 74.97 (CH, C-3), 73.88 (CH, C-5), 39.79 (C_q, $C(CH_3)_3$), 27.48 (CH_3, $C(CH_3)_3$), 24.44 (CH_3, C-2′); IR (ATR): $\tilde{\nu} = 3444$, 3061, 3031, 2971, 2920, 2872, 1730, 1493, 1477, 1452, 1395, 1365, 1344, 1280, 1226, 1207, 1160, 1100, 1068, 1049, 1035, 1016, 997, 985, 910, 876, 806, 764, 733, 702 cm^{-1}; MS (90 °C): *m*/*z* (%): 346 (2) $[M]^+$, 280 (1), 244 (1), 226 (2), 215 (3), 185 (2), 181 (7), 140 (6), 139 (68), 111 (73), 106 (19), 105 (100), 103 (21), 85 (12), 83 (15), 81 (9), 79 (10), 77 (11), 69 (10).



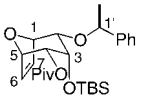
(1′*S*,1*R*,2*S*,3*R*,4*R*,5*S*)-(2-(1′-Phenylethoxy)-3-(*tert*-butyldimethylsilanyloxy)-8-oxabicyclo[3.2.1]oct-6-en-4-yl) pivaloate [(−)-22a]: Alcohol (−)-**22** (214 mg, 0.618 mmol), TBS-Cl (233 mg, 1.55 mmol) and imidazole (210 mg, 3.09 mmol) were allowed to react for 18 h as described for *rac*-**20a** to afford after column chromatography (CH/EA) (−)-**22a** (240 mg, 85 %) as a white solid. M.p. 71 °C; $[\alpha]_D^{20} = -37.3$ ($c = 1$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 7.38-7.27$ (m, 5H; Ar-H), 6.10 (dd, $J = 6.2$, 1.8 Hz, 1H; H-6), 6.01 (dd, $J = 6.2$, 1.8 Hz, 1H; H-7), 4.72 (dd, $J = 6.8$, 4.6 Hz, 1H; H-4), 4.61 (dd, $J = 4.6$, 1.8 Hz, 1H; H-5), 4.56 (q, $J = 6.5$ Hz, 1H; H-1′), 4.04 (dd, $J = 4.4$, 1.8 Hz, 1H; H-1), 3.75 (dd, $J = 6.8$, 6.7 Hz, 1H; H-3), 3.46 (dd, $J = 6.7$, 4.4 Hz, 1H; H-2), 1.48 (d, $J = 6.5$ Hz, 3H; H-2′), 1.20 (s, 9H; $C(CH_3)_3$), 0.90 (s, 9H; $SiC(CH_3)_3$), 0.15 (s, 3H; $SiCH_3$), 0.04 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 177.74$ (C_q, C=O), 144.69 (C_q, Ar-C), 132.54 (CH, C-6), 129.85 (CH, C-7), 128.59 (CH, Ar-CH), 127.96 (CH, Ar-CH), 126.44 (CH, Ar-CH), 79.67 (CH, C-2), 79.50 (CH, C-1′), 78.95 (CH, C-1), 77.15 (CH, C-5), 74.46 (CH, C-3), 74.20 (CH, C-4), 38.86 (C_q, $C(CH_3)_3$), 27.33 (CH_3, $C(CH_3)_3$), 25.84 (CH_3, $SiC(CH_3)_3$), 23.86 (CH_3, C-2′), 18.01 (C_q, $SiC(CH_3)_3$), −4.02 (CH_3, $SiCH_3$), −4.34 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3086$, 3030, 2960, 2930, 2881, 2858, 1724, 1478, 1457, 1373, 1344, 1327, 1290, 1276, 1246, 1211, 1153, 1114, 1091, 1056, 1035, 1011, 997, 980, 947, 916, 873, 835, 799, 778, 767, 736, 702 cm^{-1}; MS (100 °C): *m*/*z* (%): 403 (26) $[M - C_4H_9]^+$, 329 (1), 300 (20), 253 (10), 226 (11), 225 (59), 197 (4), 159 (14), 129 (8), 115 (8), 106 (15), 105 (100), 85 (7), 81 (61), 75 (10), 74 (31); HRMS: calcd for $C_{22}H_{31}O_5Si$: 403.1940, found: 403.1940.



(1′*S*,2*S*,3*R*,4*R*,5*S*,6*R*)-(4-(*tert*-Butyldimethylsilanyloxy)-2,6-bis-hydroxymethyl-5-(1′-phenylethoxy)-tetrahydropyran-3-yl) pivaloate [(−)-22b]: Alkene (−)-**22a** (280 mg, 0.608 mmol) in CH_2Cl_2 (7 mL) and MeOH (0.7 mL) were allowed to react as described for compound (+)-**17a** to yield after chromatography (CH/EA) (−)-**22b** (278 mg, 92 %) as a white solid. M.p. 49 °C; $[\alpha]_D^{20} = -13.2$ ($c = 1$, MeOH). NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.39-7.23$ (m, 5H; Ar-H), 4.55–4.51 (m, 1H; H-3), 4.43 (q, $J = 6.5$ Hz, 1H; H-1′), 4.06 (br dd, $J = 2.5$ Hz, 1H; H-5), 3.96 (ddd, $J = 8.2$, 3.8, 1.6 Hz, 1H; H-2), 3.86 (dd, $J = 11.8$, 7.1 Hz, 1H; H-7_a), 3.82 (dd, $J = 11.8$, 8.2 Hz, 1H; H-8_a), 3.76–3.70 (m, 1H; H-6), 3.49 (dd, $J = 11.8$, 3.8 Hz, 1H; H-8_b), 3.38 (dd, $J = 11.8$, 3.4 Hz, 1H; H-7_b), 3.02–2.99 (m, 1H; H-4), 1.43 (d, $J = 6.5$ Hz, 3H; H-2′), 1.27 (s, 9H; $C(CH_3)_3$), 0.82 (s, 9H; $SiC(CH_3)_3$), 0.14 (s, 3H; $SiCH_3$), −0.01 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 178.78$ (C_q, C=O), 142.13 (C_q, Ar-C), 128.66 (CH, Ar-CH), 128.21 (CH, Ar-CH), 126.76 (CH, Ar-CH), 76.54 (CH, C-1′), 75.54 (CH, C-6), 75.25 (CH, C-2), 73.57 (CH, C-5), 70.18 (CH, C-3), 64.76 (CH, C-4), 63.59(CH_2, C-8), 62.37 (CH_2, C-7), 39.16 (C_q, $C(CH_3)_3$), 27.34 (CH_3, $C(CH_3)_3$), 25.56 (CH_3, $SiC(CH_3)_3$), 24.11 (CH_3, C-2′), 17.70 (C_q, $SiC(CH_3)_3$), −4.93 (CH_3, $SiCH_3$), −5.11 (CH_3, $SiCH_3$); IR ($CHCl_3$): $\tilde{\nu} = 3603$, 3494, 2956, 2931, 2888, 2859, 1718, 1602, 1493, 1479, 1471, 1462, 1398, 1372, 1342, 1281, 1256, 1159, 1096, 1065, 938, 889, 841 cm^{-1}; MS (120 °C): *m*/*z* (%): 439 (4) $[M - C_4H_9]^+$, 363 (3), 259 (3), 215 (2), 201 (1), 177 (2), 169 (1), 160 (2), 159 (19), 143 (2), 129 (2), 106 (10), 105 (100), 86 (2), 76 (5), 74 (8), 70 (5); HRMS: calcd for $C_{22}H_{35}O_7Si$: 439.2152, found: 439.2152.

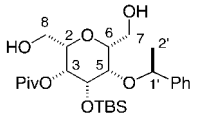


(2*S*,3*R*,4*R*,5*S*,6*R*)-(4-(*tert*-Butyldimethylsilanyloxy)-2,6-bis-hydroxymethyl-5-hydroxy-tetrahydropyran-3-yl) pivaloate [(−)-31]: Diol (−)-**22b** (256 mg, 0.516 mmol) was selectively deprotected with Pearlman's catalyst (77 mg) to afford after column chromatography (CH/EA) (−)-**31** (193 mg, 95 %) as a white solid. M.p. 115–117 °C; $[\alpha]_D^{20} = -2.8$ ($c = 1$, MeOH). NMR signals were assigned by 2D techniques: ^{1}H NMR (CD_3OD): $\delta = 4.58$ (m, 1H; H-3), 3.96 (ddd, $J = 7.6$, 4.9, 1.6 Hz, 1H; H-2), 3.88 (m, 1H; H-5), 3.86–3.79 (m, 2H; H-6, H-7_a), 3.71 (dd, $J = 11.4$ Hz, $J = 7.6$ Hz, 1H; H-8_a), 3.67–3.62 (m, 1H; H-7_b), 3.51 (dd, $J = 11.4$ Hz, $J = 4.9$ Hz, 1H; H-8_b), 3.46 (m, 1H; H-4), 1.21 (s, 9H; $C(CH_3)_3$), 0.93 (s, 9H; $SiC(CH_3)_3$), 0.18 (s, 3H; $SiCH_3$), 0.13 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 179.18$ (C_q, C=O), 77.72 (CH, C-6), 76.84 (CH, C-2), 71.40 (CH, C-3), 69.96 (CH, C-5), 69.79 (CH, C-4), 63 (CH_2, C 7), 62.64 (CH_2, C-8), 40.08 (C_q, $C(CH_3)_3$), 27.43 (CH_3, $C(CH_3)_3$), 26.20 (CH_3, $SiC(CH_3)_3$), 18.75 (C_q, $SiC(CH_3)_3$), −4.76 (CH_3, $SiCH_3$), −5.05 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3374$, 2954, 2930, 2885, 2858, 1731, 1462, 1397, 1363, 1334, 1254, 1141, 1096, 1061, 971, 925, 837, 777 cm^{-1}; MS (120 °C): *m*/*z* (%): 335 (41) $[M - C_4H_9]^+$, 259 (27), 233 (11), 216 (4), 215 (26), 197 (15), 185 (10), 177 (9), 173 (8), 171 (10), 160 (25), 159 (100), 155 (16), 147 (16), 143 (26), 141 (29), 131 (20), 129 (43), 117 (35), 85 (25), 81 (36), 77 (8), 75 (68), 73 (63), 69 (95); HRMS: calcd for $C_{14}H_{27}O_7Si$: 335.1526, found: 335.1523.

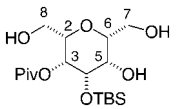


(2*α*-(1′-Phenylethoxy)-3*α*-(*tert*-butyldimethylsilanyloxy)-8-oxabicyclo-[3.2.1]oct-6-en-4*α*-yl) pivaloate (*rac*-21a): Alcohol *rac*-**21** (103 mg, 0.290 mmol), TBS-Cl (253 mg, 1.68 mmol), imidazole (145 mg, 2.13 mmol) and a catalytic amount of DMAP were allowed to react for 7 h at 90 °C as described for compound *rac*-**20a** to afford after chromatography (CH/EA) starting material *rac*-**21**(8 mg) and *rac*-**21a** (115 mg, 84 %, 91 % based on recovered starting material) as a white solid. M.p. 58 °C. NMR signals were assigned by 2D techniques: ^{1}H NMR ($CDCl_3$): $\delta = 7.37-7.24$ (m, 5H; Ar-H), 6.38 (dd, $J = 6.3$, 1.5 Hz, 1H; H-7), 6.33 (dd, $J = 6.3$, 1.7 Hz, 1H; H-6), 5.57 (m, 1H; H-4), 4.45 (q, $J = 6.5$ Hz, 1H; H-1′), 4.39 (m, 1H; H-5), 4.35 (m, 1H; H-1), 3.93 (dd, $J = 5.1$, 3.9 Hz, 1H; H-3), 3.55 (dd, $J = 4.8$, 3.9 Hz, 1H; H-2), 1.28 (d, $J = 6.5$ Hz,

3H; H-2′), 1.24 (s, 9H; $C(CH_3)_3$), 0.85 (s, 9H; $SiC(CH_3)_3$), 0.06 (s, 3H; $SiCH_3$), 0.02 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 177.91$ (C_q, C=O), 143.36 (C_q, Ar-C), 133.34 (CH, C-7), 133.03 (CH, C-6), 128.54 (CH, Ar-CH), 127.71 (CH, Ar-CH), 126.26 (CH, Ar-CH), 80.94 (CH, C-5), 79.60 (CH, C-1), 76.21 (CH, C-1′), 71.65 (CH, C-2), 68.26 (CH, C-4), 67.92 (CH, C-3), 38.92 (C_q, $C(CH_3)_3$), 27.41 (CH_3, $C(CH_3)_3$), 25.70 (CH_3, $SiC(CH_3)_3$), 24.30 (CH_3, C-2′), 18.05 (C_q, $SiC(CH_3)_3$), −4.89 (CH_3, $SiCH_3$), −5.24 (CH_3, $SiCH_3$); IR ($CHCl_3$): $\tilde{\nu} = 3085$, 2956, 2931, 2886, 2858, 1718, 1601, 1492, 1479, 1462, 1397, 1362, 1328, 1287, 1257, 1230, 1174, 1123, 1091, 1053, 1039, 1007, 967, 940, 893, 870, 842, 815 cm^{-1}; MS (110 °C): *m*/*z* (%): 403 (37) [$M - C_4H_9$]$^+$, 299 (9), 287 (13), 225 (4), 204 (3), 203 (20), 197 (4), 187 (10), 160 (4), 159 (31), 130 (2.72), 129 (22), 106 (15), 105 (100), 85 (18), 81 (7), 79 (4), 77 (3), 75(7), 73 (17); HRMS: calcd for $C_{22}H_{31}O_5Si$: 403.1940, found: 403.1940.



(4β-(*tert*-Butyldimethylsilanyloxy)-2β,6β-bis-hydroxymethyl-5β-(1′-phenylethoxy)-tetrahydropyran-3β-yl) pivaloate (*rac*-21b): Alkene *rac*-**21a** (290 mg, 0.630 mmol) in CH_2Cl_2 (7.7 mL) and MeOH (0.75 mL) were allowed to react as described for compound (+)-**17a** to yield after chromatography (CH/EA) *rac*-**21b** (280 mg, 89%) as a white solid. M.p. 59–61 °C. NMR signals were assigned by 2D techniques: ^1H NMR ($CDCl_3$): $\delta = 7.37-7.22$ (m, 5H; Ar-H), 4.90–4.84 (m, 1H; H-3), 4.56 (q, $J = 6.5$ Hz, 1H; H-1′), 4.12 (m, 1H; H-4), 3.84 (dd, $J = 11.2$ Hz, $J = 8.3$ Hz, 1H; H-8_a), 3.76 (m, 1H; H-5), 3.65 (dd, $J = 11.5$ Hz, $J = 8.6$ Hz, 1H; H-7_a), 3.60 (dd, $J = 11.2$ Hz, $J = 3.9$ Hz, 1H; H-8_b), 3.54 (m, 1H; H-2), 3.46 (m, 1H; H-6), 3.08–3.01 (m, 1H; H-7_b), 1.42 (d, $J = 6.5$ Hz, 3H; H-2′), 1.33 (s, 9H; $C(CH_3)_3$), 0.98 (s, 9H; $SiC(CH_3)_3$), 0.18 (s, 3H; $SiCH_3$), 0.11 (s, 3H; $SiCH_3$); ^{13}C NMR ($CDCl_3$): $\delta = ^{13}C$ NMR ($CDCl_3$): $\delta = 80.10$ (C_q, C=O), 144.53 (C_q, Ar-C), 129.28 (CH, Ar-CH), 128.70 (CH, Ar-CH), 128.04 (CH, Ar-CH), 82.05 (CH, C-2), 81.44 (CH, C-6), 79.77 (CH, C-1′), 76.87 (CH, C-3), 73.97 (CH, C-5), 69.97 (CH, C-4), 64.10 (CH_2, C-8), 63.83 (CH_2, C-7), 40.13 (C_q, $C(CH_3)_3$), 28.05 (CH_3, $C(CH_3)_3$), 26.80 (CH_3, $SiC(CH_3)_3$), 24.05 (CH_3, C-2′), 19.39 (C_q, $SiC(CH_3)_3$), −3.04 (CH_3, $SiCH_3$), −4.51 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} =$ 3371, 2931, 2856, 1723, 1456, 1367, 1280, 1248, 1208, 1156, 1123, 1099, 1034, 1011, 963, 943, 835, 773, 700 cm^{-1}; MS (140 °C): *m*/*z* (%): 359 (1) [$M - C_9H_{13}O$]$^+$, 335 (12), 317 (8), 233 (3), 216 (4), 215 (29), 185 (5), 171 (2), 159 (8), 147 (6), 143 (4), 129 (3), 117 (5), 106 (17), 105 (100), 85 (5), 80 (3), 77 (3), 75 (10), 73 (9); HRMS: calcd for $C_{17}H_{31}O_6Si$: 359.1889, found: 359.1891.



(4β-(*tert*-Butyldimethylsilanyloxy)-2β,6β-bis-hydroxymethyl-5β-hydroxy-tetrahydropyran-3β-yl) pivaloate (*rac*-30): Diol *rac*-**21b** (210 mg, 0.423 mmol) was deprotected with Pearlman's catalyst (64 mg) to afford after column chromatography (CH/EA) *rac*-**30** (156 mg, 94%) as a colourless solid. M.p. 135 °C. NMR signals were assigned by 2D techniques: ^1H NMR (CD_3OD): $\delta = 4.77$ (m, 1H; H-3), 4.26 (m, 1H; H-5), 3.86 (m, 1H; H-4), 3.77 (dd, $J = 11.4$ Hz, $J =$ 7.5 Hz, 1H; H-8_a), 3.73 (dd, $J = 13.05$ Hz, 9.8 Hz, 1Hz, H-7_a), 3.66 (dd, $J =$ 11.4 Hz, 4.8 Hz, 1H; H-8_b), 3.61–3.53 (m, 3H; H-2, H-6, H-7_b), 1.27 (s, 9H; $C(CH_3)_3$), 0.95 (s, 9H; $SiC(CH_3)_3$), 0.22 (s, 3H; $SiCH_3$), 0.17 (s, 3H; $SiCH_3$); ^{13}C NMR (CD_3OD): $\delta = 179.68$ (C_q, C=O), 81.66 (CH, C-2), 81.56 (CH, C-6), 74.86 (CH, C-3), 71.78 (CH, C-5), 70.28 (CH, C-4), 62.91 (CH_2, C-8), 63 (CH_2, C-7), 40.01 (C_q, $C(CH_3)_3$), 27.72 (CH_3, $C(CH_3)_3$), 26.49 (CH_3, $SiC(CH_3)_3$), 19.03 (C_q, $SiC(CH_3)_3$), −4.01 (CH_3, $SiCH_3$), −4.11 (CH_3, $SiCH_3$); IR (ATR): $\tilde{\nu} = 3397$, 2931, 2858, 1732, 1471, 1435, 1391, 1367, 1283, 1246, 1154, 1114, 1099, 1057, 999, 956, 919, 894, 859, 836, 779 cm^{-1}; MS (150 °C): *m*/*z* (%): 335 (28) [$M - C_4H_9$]$^+$, 317 (32), 251 (14), 233 (15, 216 (2), 215 (75), 197 (10), 185 (11), 173 (9), 171 (16), 159 (23), 155 (13), 147 (55), 143 (56), 141 (11), 131 (14), 129 (32), 117 (60), 85 (41), 81 (12), 77 (10), 75 (86), 73 (75), 69 (100); HRMS: calcd for $C_{14}H_{27}O_7Si$: 335.1526, found: 335.1525.

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  0947-6539/01/0722-4788 $ 17.50+.50/0

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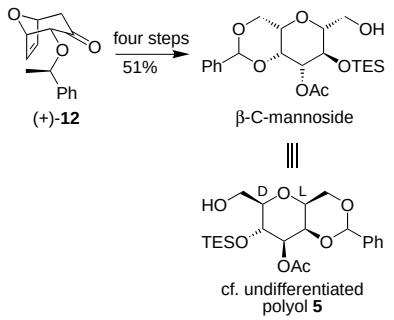

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