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Synthesis of highly oxygenated decalins from sugar allyltins: an access to sulfur and phosphorus derivatives

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ABSTRACT

A sugar allyltin derivative (with the D-*gluco*-configuration) was converted into D-*xylo*-dienoaldehyde and then into several bicyclic highly oxygenated compounds. The proposed methodology allows for a convenient synthesis of such derivatives containing heteroatoms other than oxygen. Molecular docking studies employing AutoDock 4.2 and AutoDock Vina were conducted in order to evaluate their activity as glycosidase inhibitors.

1. Introduction

Cyclic polyhydroxylated compounds, which are structurally similar to carbohydrates, act as glycomimetics; they are recognized by appropriate enzymes but due to them not being metabolized, block their active center(s).[1] Usually, they have a mono- or bi-heterocyclic structure or a mono-carbocyclic structure. Most known derivatives of this type are iminosugars[2] (inhibitors of glycosidases); representatives of this class (Glyset™, Zavesca™) have found application in clinical use. Simple monocarbocyclic derivatives (conduritols,[3] cyclophellitols,[4] inositols,[5] and carbasugars[6]) also possess potent biological activities.

Much less is known about the synthesis and properties of polyhydroxylated bicyclic derivatives, although such compounds can act as sugar mimics.[7,8] The bicyclic structure can also be found in some antibiotics (e.g., nodusmicin, nargenicin, and branimycin).[9–11]

Most common bicyclic structures are represented by decalin and hydrindane scaffolds (although derivatives with bicyclo[4.2.0]octane[12a] and bicyclo[2.2.2]octane[12b] skeletons are also known) which strongly resemble natural inhibitors of glycosidases (Fig. 1).[7c,8,13] Polyhydroxylated bicyclic derivatives may also be regarded as carbasugars with a rigid structure.

Very often such products are prepared as a racemic mixture.[14] Much more valuable, however, are enantiomerically pure derivatives. There are two routes to such compounds. In the first one, the optically inactive material is converted into pure enantiomers either by kinetic resolution of a racemate[15] or desymmetrization of meso-derivatives at the early stage of the synthesis. The second, the more convenient method involves the application of enantiomerically pure substrates. In the Roush[10] synthesis of nargenicins, intramolecular Diels–Alder (IMDA) cyclization of the corresponding triene **1** was a key step, while Mulzer[11] applied the ring closing metathesis reaction (RCM) in the synthesis of branimycin (Fig. 2).

The trienes used in the syntheses of Roush and Mulzer were prepared in a number of steps from simple synthons (D-glyceraldehyde and quinic acid). It seems however, to be more convenient to initiate the synthesis from simple sugars. For the construction of precursors of type **1**, Herczegh applied pentoses or hexoses, which by using classical sugar chemistry, were converted into the target trienes as a mixture of geometrical isomers (Fig. 3).[16]

Our approach to such bicyclic systems was based on a stereocontrolled fragmentation of sugar allyltins **2**, which provided the corresponding dienoaldehydes **3** exclusively with the *E*-geometry across the double bond.[17] The reaction of such synthons with stabilized Wittig reagent afforded trienes which underwent the IMDA reaction under high pressure to afford perhydroindenes **5** (Fig. 4).[18,19]

Alternatively, aldehyde **3** was converted into phosphonate **4**, which when reacted with an aldehyde furnished another triene undergoing spontaneous cyclization to decalin **5**.[19,20] Both synthons are convenient starting materials for the preparation of fully hydroxylated decalins and perhydroindanes. In order to achieve this goal, an oxidation of the allylic position is required, as well as the oxidation of the double bond and replacement of the C-substituent for a heteroatom. As we have found, direct oxidation of the allylic position was not possible, however oxidation of the double bond (epoxidation, *cis*-dihydroxylation) of both types of synthons provided the corresponding derivatives in good yield.[21]

Precursor **7**[20] can be selectively converted either into *cis*-diol **8** or a mixture (2:1) of epoxides.[21] The introduction of the oxygen functionality at the allylic position was done 'indirectly', that is, by reaction of the epoxides with selenide followed by oxidative work-up (Scheme 1).[22] Herein, further functionalization of compounds of type **6** will be presented. Furthermore, molecular

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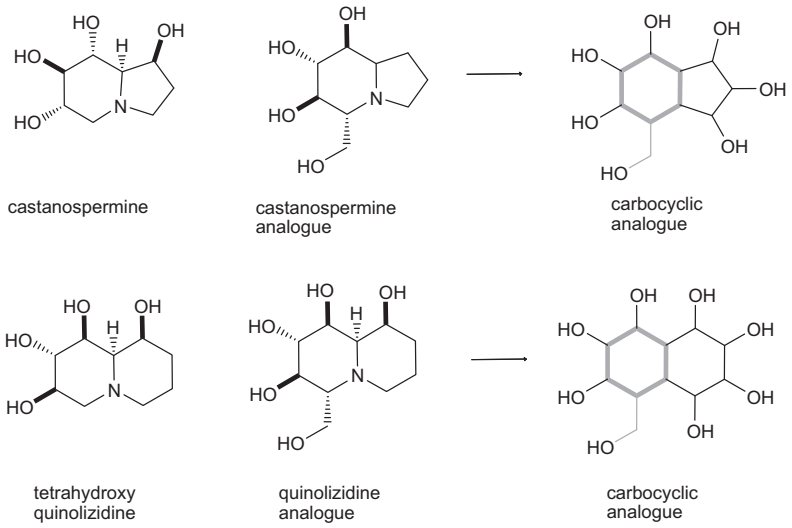


Figure 1. Similarity of the polyhydroxylated carbobicyclic derivatives to bicyclic iminosugars and monocyclic carbasugars with rigid structure.

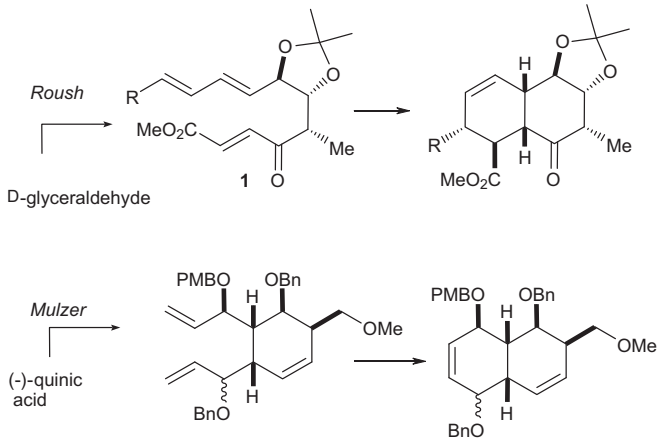


Figure 2. Approach to highly functionalized decalins by Roush and Mulzer.

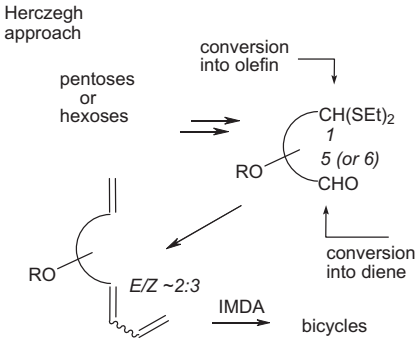


Figure 3. Herczegh approach to highly oxidized bicycles from sugars.

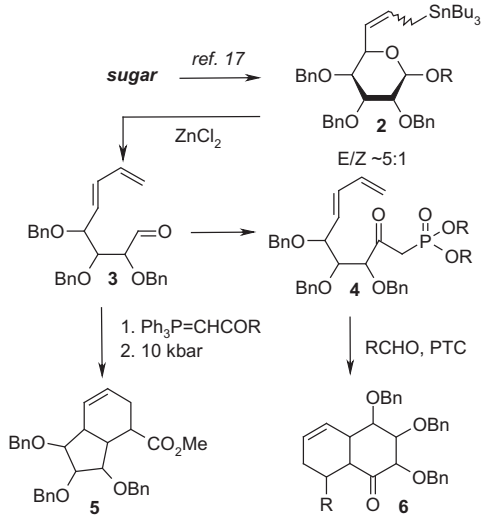


Figure 4. Synthesis of highly oxygenated bicycles from sugar allyltins.

docking studies allowed for a preliminary evaluation of the compounds obtained as glycosidase inhibitors.

2. Results and discussion

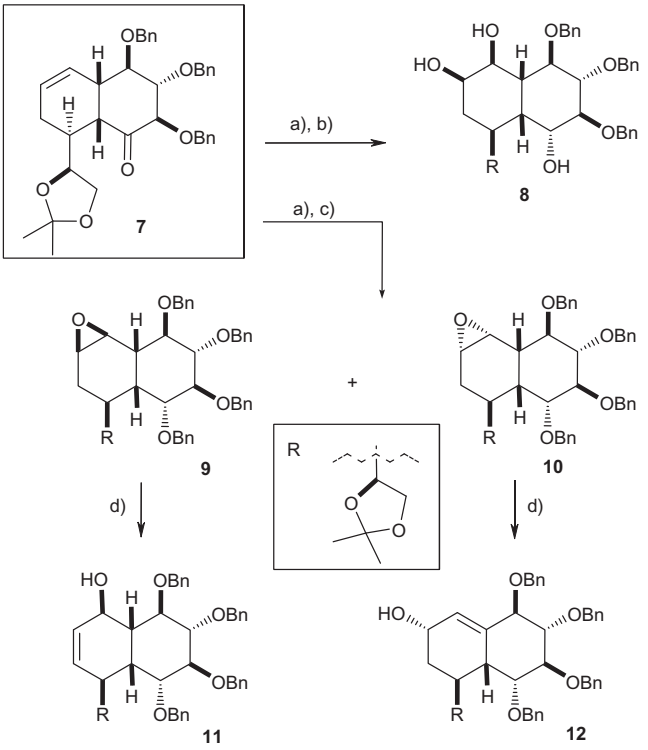
Functionalization of precursor **11** requires oxidation of the double bond and cleavage of the terminal diol grouping (C1′–C2′). Thus, alcohol **11** was protected as benzyl ether **13** and subjected to hydrolysis. The expected compound **14** seemed to be a convenient precursor of the target olefin **17**; moreover, the carbonyl group in the intermediate compound **16** could be cleaved under the Baeyer Villiger conditions to afford the C-9 hydroxylated derivative.

However, treatment of olefin **13** with dilute sulfuric acid afforded cyclic derivative **15** as the main product and only relatively small amounts of the expected diol **14** were obtained (Scheme 2).

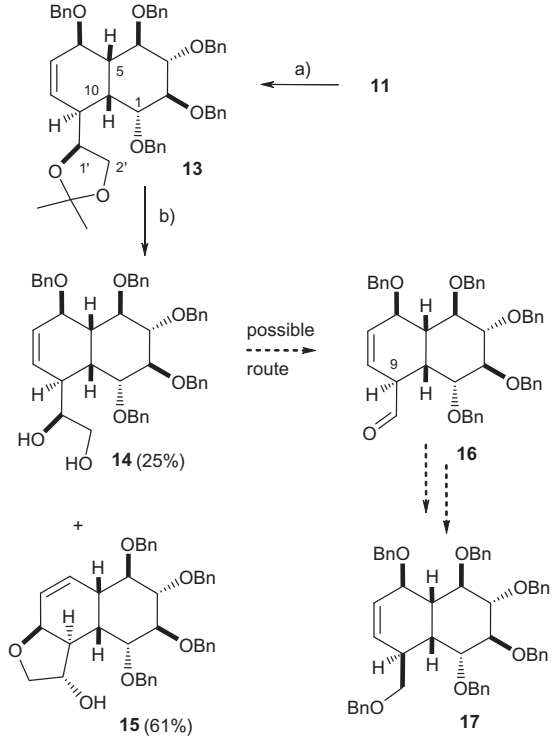
The structure of this unexpected tricyclic derivative was elucidated on the basis of the NOESY spectra in which the cross-peaks between H8–H9, H1′–H10, and H5–H10 were observed (Fig. 5)

The synthesis of compound **17** was therefore realized via an alternative route (Scheme 3). Hydrolysis of the isopropylidene unit in compound **7** afforded the corresponding diol **18** which was subjected to periodate cleavage to provide aldehyde **19**. Reduction of this compound furnished alcohol **20**, and then finally converted into **21**, which was stable under basic conditions.

Oxidation of the allylic position in **21** was also performed 'indirectly' as for compound **7**. Epoxidation of the double bond under standard conditions provided two epoxides: **22** and **23** in a 1:1 ratio; both oxiranes were converted into the allylic alcohols **24** and



Scheme 1. (a) $NaBH_4$; (b) OsO_4 (cat.), NMMO; (c) (i) BnBr, NaH, DMF; (ii) mCPBA; (d) PhSeSe/$PhNaBH_4$ then H_2O_2.



Scheme 2. (a) BnBr, NaH, and DMF (60%); (b) H_2SO_4, H_2O, and THF.

25, respectively, by reaction with the selenide anion followed by oxidative work-up (Scheme 4).

The structures of these allylic alcohols were also proven by the NOESY NMR spectra of their acetates. In the spectrum of **24-Ac**, the

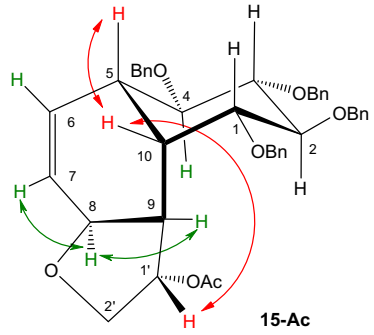
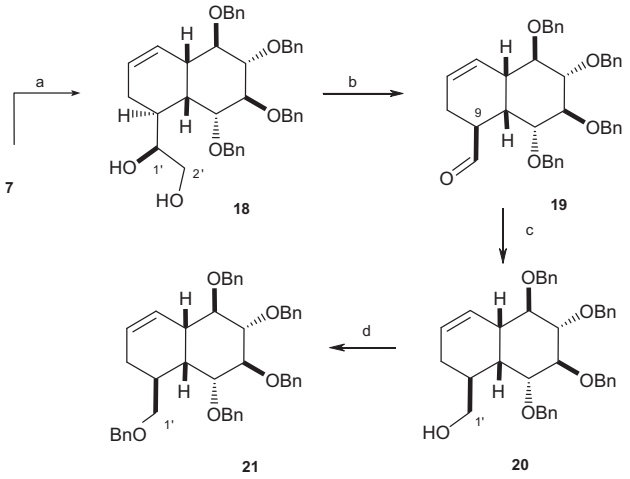


Figure 5. Important NOESY interactions in the acetate **15-Ac**.



Scheme 3. (a) HCl, EtOH, H_2O, and THF (71%); (b) (i) $NaIO_4/SiO_2$, CH_2Cl_2; (ii) $NaBH_4$, MeOH (86%); (c) NaH, BnBr, and THF (90%).

H6 proton correlated to H5 and, which is most important, to H4. The latter correlation confirmed the proposed structure. A correlation between the protons from the acetyl group at C-6 and the benzyl group at C-1′ was also observed (Fig. 6).

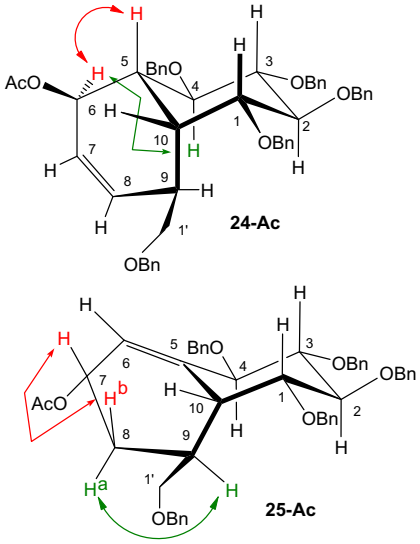
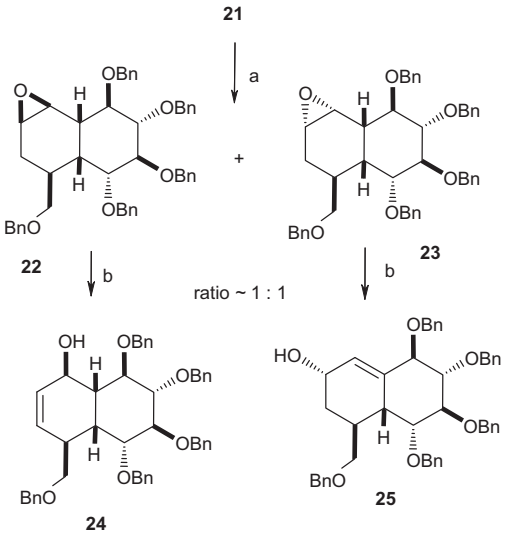
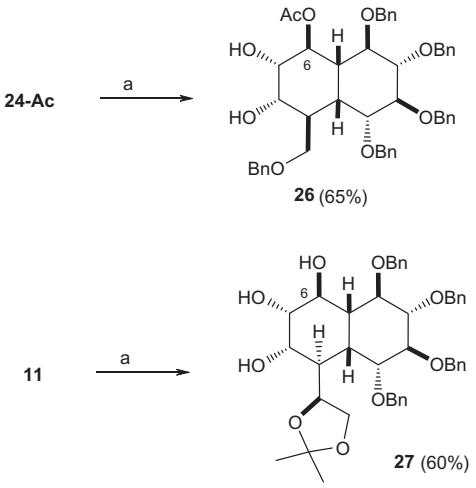


Figure 6. Important NOESY interactions in the acetates **24-Ac** and **25-Ac**.



Scheme 4. (a) *m*-CPBA, CH_2Cl_2, 3 °C, 67%; (b) (i) PhSeSePh, $NaBH_4$; (ii) H_2O_2.



Scheme 5. (a) OsO_4 (cat), NMMO, THF, and *t*-BuOH.

The structure of the **25-Ac** was proposed on the basis of the observed cross peaks between pairs: H7–H8b and H8a–H9, which strongly suggested that they were in the *cis*-relationship.

Functionalization of the double bond in olefins **11** and **24-Ac** provided the polyhydroxylated derivatives **26** and **27** (Scheme 5) as single products. This was rather surprising since the stereoselectivity of the *cis*-dihydroxylation of the double bond is usually sensitive to the oxygen functionality at the α-position (the alkoxy or hydroxy groups usually secure a much higher selectivity than the ester functions,[23] that is, at the C-6 position).

The structures of both compounds **26** and **27** were assigned from advanced NMR experiments. We have observed the NOE interaction between H7 and H10. This strongly suggested that two new hydroxyls were introduced (Fig. 7) from 'the bottom' of the molecule, since in the alternative structure, such a correlation is not possible.

Moreover, the distance between these two protons in **26** or **27** in the chair conformation is rather large; thus the presence of this interaction suggests that the 'left' ring is distorted. This assumption was supported by coupling constants. The $J_{6,7}$ value in the chair conformation (where both H6 and H7 would be equatorial) should

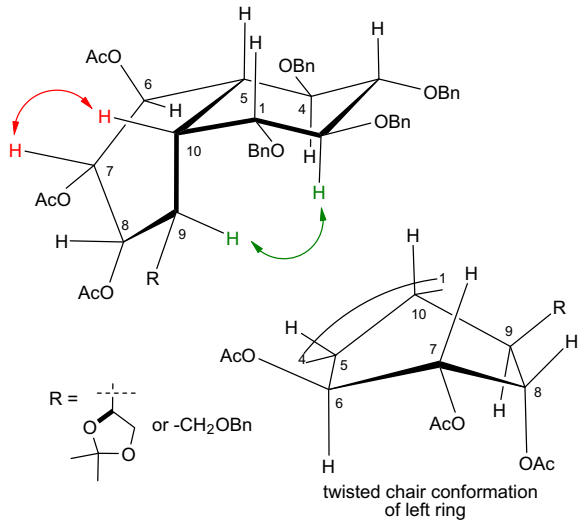
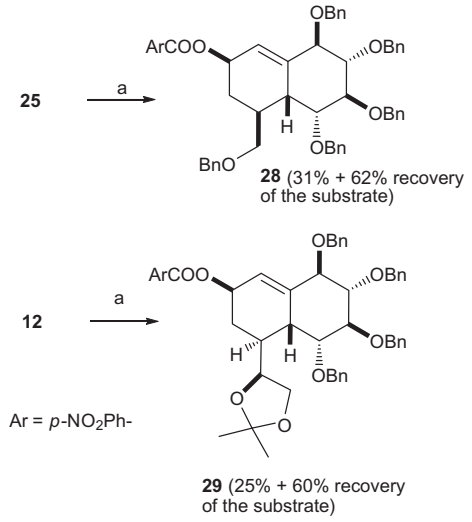


Figure 7. Important NOESY interactions in the triacetates **26-Ac3** and **27-Ac3**.

be much smaller than that observed (6.5 Hz). On the other hand, the H8 and H9 protons in the chair conformation would be axial, so the $J_{8,9}$ value should be about 10 Hz. We observed, however, J = 6.7 Hz, which seems to prove the proposed distortion of the 'left ring'.

The other set of stereoisomeric compounds of this type was available by inversion of the configuration at the carbinol center under Mitsunobu conditions. Treatment of allylic alcohols **12** with *p*-nitrobenzoic acid, DIAD, and triphenylphosphine afforded the expected S_N2 product **29**. Similarly, treatment of alcohol **25** led to **28** (Scheme 6).



Scheme 6. (a) p-$NO_2C_6H_4COOH$, DIAD, and PhP_3.

Although in such complex products (e.g., **11**) an S_N2' process might be observed[22] under Mitsunobu conditions, both reactions performed for **12** and **25** afforded only the S_N2 products (albeit in low yield: ~60% of the starting material was recovered in both cases). No S_N2' products were formed probably because of the hindered *syn* trajectory required for this substitution of the double bond.[23]

The configuration of products obtained was confirmed by the NOESY correlations (Fig. 8). Two systems of correlating protons were detected for both products **28** and **29**: H-8b, H-10, and H-1 and the second one: H7, H8a, H9, and H2. Such correlations fully support the proposed structures.

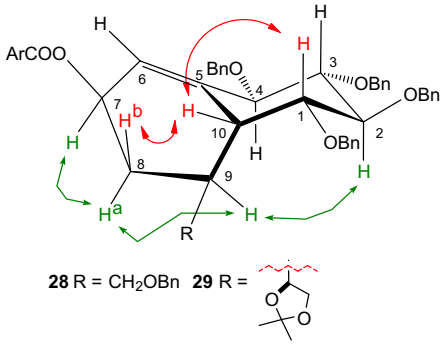


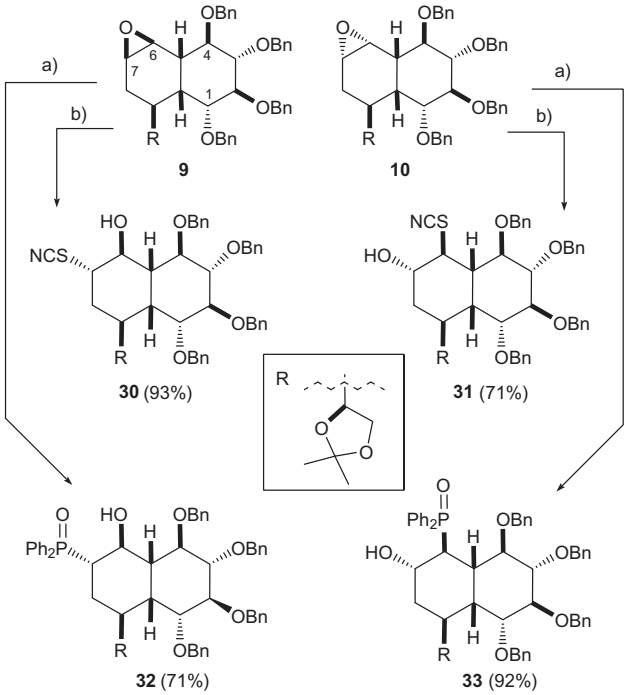
Figure 8. Diagnostic NOESY interactions in derivatives **28** and **29**.

The highly regioselective opening of the oxirane ring in compounds **9** and **10** might open up a convenient route to derivatives containing heteroatoms other than oxygen or nitrogen placed on the decalin ring; we decided to check the possibility of introducing sulfur and phosphorus nucleophiles. The treatment of epoxide **9** with an ether solution of HSCN[24] afforded thiocyanate **30** as the single product (Scheme 7).

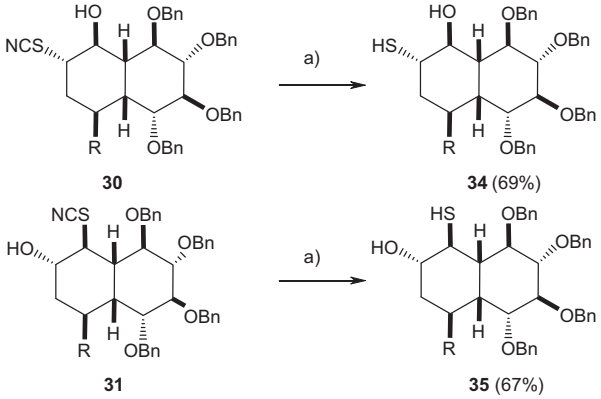
Alternatively, opening of the oxirane ring with the phosphide anion [(PPh_2^-)[25]] provided the corresponding phosphine. Although this reaction was performed under an argon atmosphere, we observed the formation of significant amounts of the phosphine oxide.[26] After exposing the reaction mixture to air, the full conversion to phosphine oxide **32** (Scheme 7) was noted.

The same sequence of reactions performed on the diastereoisomeric epoxide **10** provided the thio-cyanate **31** and phosphine oxide **33**, respectively. The determination of the configurations of all compounds was based on 1D NOE experiments.

As expected on the basis of the Fürst/Plattner rule,[27] the configuration of the products was *trans*-diaxial; the attack of the nucleophile (either SCN^- or Ph_2P^-) occurred at the C7 carbon atom in epoxide **9** and at the C6 atom in the alternative oxirane **10**. This regioselectivity of the opening of the three membered ring in similar *cis*-decalins has been previously observed.[21]



Scheme 7. (a) (i) Ph_2PK, THF; (ii) O_2 (air); (b) HSCN, Et_2O.



Scheme 8. (a) $LiAlH_4$, THF.

It is reported that the treatment of thiocyanates with Grignard reagents provides the corresponding dialkyl sulfides in good yields. This methodology was successfully applied to the preparation of glycosyl sulfides, important starting materials in the synthesis of oligosaccharides.[28a] However, this reaction, besides the desired dialkyl sulfides, also afforded significant amounts of the thiols (resulting from reductive removal of the CN moiety).[28a,b]

In order to avoid the formation of a mixture (thiol/dialkyl sulfide), an alternative transformation can be used which is based on the reduction of thiocyanates with lithium aluminum hydride. Treatment of bicyclic derivatives **30** and **31** with $LiAlH_4$ afforded the desired thiols **34** and **35** in good yields (Scheme 8).

In the NMR spectra of **30**, **31**, **32**, **34,** and **35** recorded at room temperature, broad signals were observed due to relatively slow conformational changes, which disappeared at an elevated (80 °C) temperature (see Section 4).

Since in the 'right' ring all of the benzyloxy groups are equatorial, it seems rather unlikely for the whole molecule to undergo typical *cis*-decalin ring inversion, so this phenomenon results (most probably) rather from the conformational mobility (chair and twisted chair) of the 'left' ring.

2.1. Molecular docking

Compounds **27**, **32**, **33**, **34,** and **35** can be regarded as precursors for structures **27a**, **32a**, **33a**, **34a**, and **35a** (Fig. 9) which can be seen as potential glycosidase inhibitors. The AutoDock 4.2[29] and AutoDock Vina[30] programs were used to perform docking studies (see Section 4) on several human glycosidases which structures were found at http://www.pdb.org. For our studies, we chose those already containing a ligand known for its inhibitory activity.[†] The most promising results were obtained for human pancreatic α-amylase (PDB ID:1U33), human lysosomal acid-β-glucosidase (PDB ID:2NSX), and 3GXF) and human ER α-mannosidase I (PDB ID:1FO3) (Table 1). The ligands present in these structures were also subjected to docking ('ligand', Table 1).

Comparing the results from AutoDock 4.2, **32a**, and **33a** gave significantly better results than the other derivatives. They showed slightly smaller (1U33, 2NSX, and 3GXF) or even higher (1FO3) affinities than known inhibitors. A similar tendency was observed using AutoDock Vina: again, **32a** and **33a** seemed to be the best binding derivatives.[‡] Most probably, the phenyl rings present in these structures contribute significantly to the van der Waals term in AD's free energy force field. Visual analysis of the lowest energy

[†] The ligand was assumed to be bound in the enzyme's active site.

[‡] Differences in energy values result from the fact that Vina uses different scoring functions than AD 4.2.

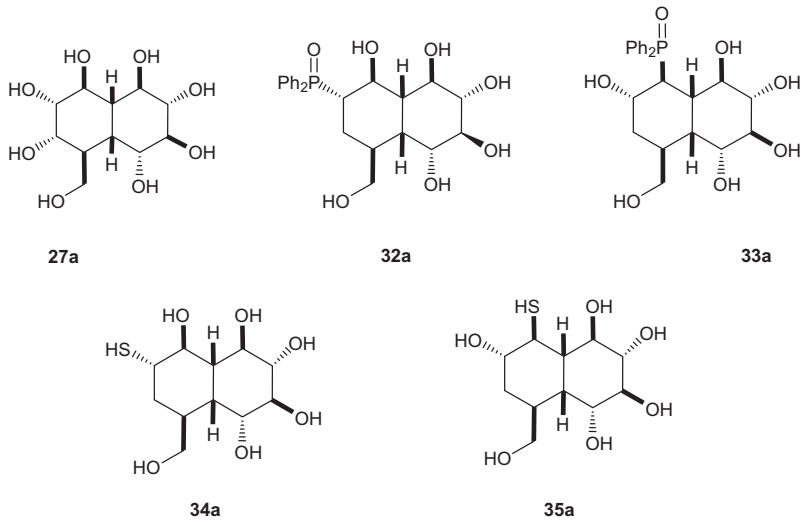


Figure 9. Structures subjected to molecular docking.

Table 1
Results of the molecular docking studies

	1U33		2NSX		1FO3		3GXF	
	AD 4.2	Vina	AD 4.2	Vina	AD 4.2	Vina	AD 4.2	Vina
Ligand[a]	−8.66[b] (−7.15[c])	−9.2[d]	−8.05 (−7.67)	−5.8	−6.02 (−5.03)	−6.8	−8.29 (−7.86)	−5.9
27a	−6.45 (−5.20)	−7.3	−5.92 (−4.73)	−6.6	−6.39 (−4.93)	−7.5	−6.43 (−4.49)	−6.6
32a	−8.47 (−7.41)	−8.1	−7.74 (−6.21)	−7.5	−7.77 (−7.10)	−7.8	−7.88 (−6.12)	−7.6
33a	−7.78 (−6.74)	−7.9	−7.90 (−6.53)	−8.0	−7.64 (−6.37)	−7.4	−8.15 (−6.69)	−8.0
34a	−7.21 (−5.55)	−6.7	−6.64 (−5.81)	−6.4	−6.43 (−5.75)	−6.7	−6.67 (−4.79)	−5.9
35a	−7.19 (−5.64)	−7.0	−6.79 (−5.21)	−6.1	−5.85 (−5.17)	−6.5	−6.86 (−4.94)	−6.1

All values are presented in kcal/mol. Structures 2NSX and 3GXF represent the same enzyme complexed with isofagomine but at different pH values (4.5 and 7.5, respectively). Standard error is ~2.5 kcal/mol.

[a] Binding energy of the ligand present in the PDB structure.
[b] The lowest binding energy obtained.
[c] Mean binding energy of the lowest energy cluster.
[d] For Vina, only the best result is presented.

binding poses demonstrates that compounds **27a** and **32a**–**35a** bind in the same pocket as the ligand from the PDB structure. The only exception was observed in case of 3GXF for **33a** when using Vina.

Overall, the docking studies indicated that structures **32a** and **33a**, among those shown in Table 1, seem to be especially good inhibitors of human enzymes related to carbohydrate metabolism.

3. Conclusion

In conclusion, we have demonstrated a useful methodology, which allows us to prepare, in a predictable way, highly oxygenated decalins from convenient precursors obtained directly from sugar allyltins. Using the route presented herein, derivatives containing phosphorus or sulfur units are made available. Furthermore, we have demonstrated, via molecular docking studies, that the latter can be regarded as potential glycosidase inhibitors.

4. Experimental

4.1. General experimental methods

The NMR spectra were recorded with a Varian 600 MHz or Bruker 500 MHz in $CDCl_3$ at 25 °C unless otherwise stated. The structures were assigned, whenever necessary, with the help of 2D correlation experiments (COSY, HSQC, HMBC, and NOESY). Chemical shifts were reported with reference to TMS (^1H) or H_3PO_4 (^{31}P). Optical rotations were measured with a Jasco P 1020 polarimeter (sodium light). The IR spectra were recorded with a Perkin Elmer Spectrum 2000 instrument. All MS spectra were recorded with a Mariner PerSeptive Biosystems spectrometer. Thin layer chromatography was performed on pre-coated plates (0.25 mm, silica gel 60 F_{254}). Column chromatography was carried out with silica gel (230–400 mesh).

4.2. (1*R*,2*R*,3*S*,4*R*,5*R*,6*R*,9*S*,10*R*)-1,2,3,4,6-Pentabenzyloxy-9-[(4′*R*)-2′,2′-di methyl-1′,3′-dioxolane-4′-yl]bicyclo[4.4.0]dec-7,8-ene 13

To a vigorously stirred solution of **11** (178 mg, 0.26 mmol) in DMF (5 mL), imidazole (3 mg, 45 μmol) and sodium hydride were added in one portion (11 mg, 0.52 mmol). After 15 min. benzyl bromide (0.1 mL, 1 mmol) was added, the mixture was stirred for 1 h at rt (TLC monitoring in hexane/EtOAc, 3:1) after which the reaction was quenched with saturated aqueous $NaHCO_3$ (15 mL). The product was extracted with EtOAc (4 × 30 mL), the organic layer was washed with brine (30 mL), dried, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc, 10:1) afforded compound **13** as a colorless oil (118 mg, 60%). $[\alpha]_D^{22} = -11.2$ (*c* 1, $CHCl_3$); *m*/*z* = 789.4 ($[M+Na]^+$); ^1H NMR (500 MHz) δ: 6.05 (1H, dd, $J_{8,7}$ = 10.2 Hz, $J_{8,9}$ = 2.9 Hz, H-8), 5.86 (1H, m, H-7), 5.04 (1H, m, H-1′), 4.93–4.36 (10H, OCH_2Ph), 4.04 (1H, dd, *J* = 5.4 Hz, *J* = 2.1 Hz, H-6), 3.84–3.78 (2H, d and d,

J = 9.9 Hz, J = 6.9 Hz, H-2, H-2′a), 3.70 (1H, app. t, J = 7.4 Hz, H-2′b), 3.48–3.54 (1H, dd, $J_{1,10}$ = 6.8 Hz, $J_{1,2}$ = 10.2 Hz, H-1), 3.53 (1H, app. t, $J_{2,3}$ = 10.1 Hz, H-3), 3.34 (1H, dd, $J_{3,4}$ = 11.5 Hz, $J_{4,5}$ = 9.1 Hz, H-4), 2.72 (1H, m, H-9), 2.17 (1H, dt, $J_{5,10}$ = 6.4 Hz, $J_{9,10}$ = 10.6 Hz, H-10), 1.93 (1H, m, H-5), 1.42 and 1.19 ppm (6H, 2 × s, C(CH_3)$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C) δ: 130.5 (C-8), 126.4 (C-7), 108.4 (C(CH_3)$_2$), 86.6 (C-3), 83.9 (C-1), 82.7 (C-2), 78.7 (C-4), 75.99 (C-1′), 75.96, 75.8, 75.1, 73.6, and 70.3 (5 × OCH_2Ph), 69.3 (C-6), 64.9 (C-2′), 41.6 (C-5), 37.1 (C-9), 32.1 (C-10), 26.0 and 24.4 ppm (C(CH_3)$_2$). Anal. Calcd for $C_{50}H_{54}O_7$: C 78.3, H 7.1. Found: C 78.3, H 6.9%.

4.3. Removal of the isopropylidene protecting group from 13

To a solution of **13** (118 mg, 0.154 mmol) in THF (15 mL), H_2SO_4 (17% aqueous solution, 6 mL) was added slowly and the mixture was heated at reflux until all of the starting materials were consumed (5 h; TLC monitoring). The reaction was quenched with saturated aqueous $NaHCO_3$ (50 mL) and the product was extracted with EtOAc (5 × 20 mL). The organic layer was washed with brine (30 mL), dried, concentrated, and the residue was purified by column chromatography (hexane/EtOAc, 3:1) to afford compound **14** (28 mg, 25%) and compound **15** (58 mg, 61%), characterized as acetate **15-Ac**, as a colorless oil.

4.3.1. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,9*S*,10*R*)-1,2,3,4,6-Pentabenzyloxy-9-[(4′*R*)-1′,2′-dihydroxyeth-1′-yl]bicyclo[4.4.0]dec-7,8-ene 14: *m*/*z* = 749.8 ([M+Na]$^+$)

Compound ***15-Ac***: $[\alpha]_D^{22} = +171.2$ (c 1, $CHCl_3$); m/z = 683.3 ([M+Na]$^+$). ^{1}H NMR (600 MHz) δ: 6.20 (1H, ddd, $J_{6,8}$ = 1 Hz, $J_{6,5}$ = 5.9 Hz, $J_{6,7}$ = 9.9 Hz, H-6), 5.99 (1H, m, H-1′), 5.91 (1H, dd, $J_{7,8}$ = 3.9 Hz, H-7), 4.39 (1H, t, $J_{8,9}$ = 4.7 Hz, H-8), 4.09 (1H, dd, $J_{1',2'}$ = 4.6 Hz, $J_{2',2'}$ = 10.6 Hz, H-2′), 3.98 (1H, t, $J_{2,3}$ = $J_{1,2}$ = 9.5 Hz, H-2), 3.75–3.25 (1H, dd, $J_{1',2'}$ = 1.9 Hz, H-2′), 3.64 (1H, dd, $J_{1,10}$ = 4.6 Hz, $J_{1,2}$ 9.9 Hz, H-1), 3.55 (1H, t, $J_{3,4}$ = 9.1 Hz, H-3), 3.39 (1H, dd, $J_{4,5}$ = 10.9 Hz, H-4), 2.45 (1H, ddd, $J_{1',9}$ = 5.8 Hz, $J_{9,10}$ = 12.8 Hz, H-9), 2.22 (1H, m, H-5), 2.03 (3H, s, CH_3CO), 2.02 ppm (1H, m, H-10). ^{13}C NMR (150 MHz) δ: 170.4 (CH_3CO), 132.7 (C-6), 125.9 (C-7), 86.4 (C-3), 83.5 (C-4), 82.9 (C-1), 81.9 (C-2), 78.6 (C-1′), 73.6 (C-8), 71.1 (C-2′), 42.8 (C-9), 39.2 (C-5), 34.1 (C-10), 21.1 ppm (CH_3CO).

4.4. Removal of the isopropylidene protecting group from 7

To a solution of **7** (4.11 g, 6.23 mmol) in THF (50 mL), 5% aqueous HCl (20 mL) was slowly added and the reaction mixture was heated at reflux. After 3 h (TLC monitoring), the reaction was quenched with saturated aqueous $NaHCO_3$ (30 mL) and the product was extracted with EtOAc (3 × 30 mL). The organic layer was washed with brine (30 mL), dried, concentrated, and the product was purified by column chromatography (hexane/EtOAc, 3:1) to afford diol **18** as a colorless oil (2.71 g, 71%), which was characterized as a diacetate.

4.4.1. (1*R*,2*R*,3*S*,4*R*,5*R*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-9-((1′*R*)-1′,2′-diacetyloxy-eth-1′-yl)bicyclo[4.4.0]dec-6,7-ene 18-(Ac)$_2$: *m*/*z* = 643.3 ([M+Na]$^+$)

^{1}H NMR (500 MHz) δ: 5.98–5.90 (2H, m, H-6, H-1′), 5.75–5.70 (1H, m, H-7), 5.06–4.55 (8H, OCH_2Ph), 4.18–4.10 (3H, m, 2 × H-2′, H-2), 3.61 (1H, dd, $J_{1,10}$ = 4.2 Hz, $J_{1,2}$ = 10.3 Hz, H-1), 3.57–3.48 (2H, m, H-3,4), 2.35–2.20 (4H, m, H-5, H-8a, H-9, H-10), 2.09 (3H, s, CH_3CO), 1.97–1.85 (1H, m, H-8b), 1.78 ppm (3H, s, CH_3CO). ^{13}C NMR (125 MHz) δ: 128.3–127.7 (C-5,6 and C arom.), 86.8 and 84.8 (C-3,4), 83.4 (C-1) 81.8 (C-2), 75.7, 75.6, 75.5, and 75.1 (4 × OCH_2Ph), 72.8 (C-1′), 63.1 (C-2′), 40.6 (C-5), 39.3 (C-9), 35.6 (C-10), 26.7 (C-8), 21.2 and 20.7 ppm (2 × CH_3CO).

4.4.2. (1*R*,2*R*,3*S*,4*R*,5*R*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-9-hydroxymethylbicyclo[4.4.0]dec-6,7-ene 20

To a vigorously stirred solution of the diol **18** (2.71 g, 4.4 mmol) in dichloromethane (100 mL) containing small amounts of water (1 mL), $NaIO_4$ adsorbed on silica gel (11.5 g of SiO_2, with approximately 7 mmol of $NaIO_4$)[31] was added in portions and stirring was continued for 4 h (TLC monitoring in hexane/EtOAc, 3:1). Next, the solid was filtered off and the filtrate was concentrated to afford crude aldehyde **19** (2.31 g), which was used directly in the next step.

Aldehyde **19** (2.31 g, 3.93 mmol) was dissolved in a THF/methanol/water mixture (30 + 30 + 5 mL) to which $NaBH_4$ (260 mg, 7 mmol) was added in portions. After 3 h (TLC monitoring in hexane/EtOAc, 3:1) saturated aqueous $NaHCO_3$ (20 mL) was added and the solvent was removed in vacuo. The residue was partitioned between water (50 mL) and EtOAc (30 mL), the organic phase was separated, and aqueous phase extracted with EtOAc (3 × 30 mL). The combined organic solutions were washed with brine, dried, and the product was isolated by column chromatography (hexane/EtOAc, 4:1–3:1) to afford **20** as a colorless oil (2.27 g, 86% from the diol), which was characterized as acetate **20-Ac**.

4.4.3. (1*R*,2*R*,3*S*,4*R*,5*R*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-9-acetyloxymethyl bicyclo[4.4.0]dec-6,7-ene 20-Ac

$[\alpha]_D^{22} = +103.7$ (c 1, $CHCl_3$); m/z = 655.5 ([M+Na]$^+$). ^{1}H NMR (500 MHz) δ: 5.96 (1H, m, H-6), 5.73 (1H, m, H-7), 4.74–4.65 (3H, m, H-1a′,OCH_2Ph), 4.09 (1H, dd, $J_{9,1'b}$ = 7.3 Hz, $J_{1'a,1'b}$ = 11 Hz, H-1b′), 3.85 (1H, m, $J_{1,2}$ = 9.2 Hz, H-2), 3.61–3.53 (3H, m, H-1, H-3, H-4), 2.36–2.28 (1H, m, H-8a), 2.25–2.15 (3H, m, H-5, H-9, H-10), 1.95 (3H, s, COCH_3), 1.94–1.87 ppm (1H, m, H-8b). ^{13}C NMR (125 MHz; $CDCl_3$, 25 °C) δ: 171.1 (COCH_3), 128.3 (C-5), 126.9 (C-6), 128.4–127.2 (C arom.), 86.6 (C-1), 84.8 (C-3), 83.5 (C-4), 81.6 (C-2), 67.4 (C-1′), 39.9 (C-5), 38.3(C-10), 32.5 (C-9), 30.7 (C-8), 20.8 ppm (COCH_3). Anal. Calcd for $C_{39}H_{42}O_5$ + H_2O: C 77.0, H 7.3. Found: C 76.8, H 7.1%.

4.4.4. (1*R*,2*R*,3*S*,4*R*,5*R*,9*S*,10*R*)-1,2,3,4,Tetrabenzyloxy-9-benzyloxymethylbicyclo[4.4.0]dec-6,7-ene 21

To a vigorously stirred solution of **20** (2.27 g, 3.84 mmol) in DMF (30 mL) imidazole (15 mg, 225 μmol) and sodium hydride (163.5 mg, 7.7 mmol) were added in one portion. After 15 min. benzyl bromide (1.5 mL, 15 mmol) was added and the mixture was stirred for 1 h (TLC monitoring in hexane/EtOAc, 3:1). Saturated aqueous $NaHCO_3$ (15 mL) was added, the product was extracted with EtOAc (4 × 30 mL), the organic layer was washed with brine (30 mL), dried, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc, 10:1) afforded compound **21** as a colorless oil (2.36 g, 90%). $[\alpha]_D^{22} = +71.0$ (c 1, $CHCl_3$); m/z = 703.4 ([M+Na]$^+$), ^{1}H NMR (500 MHz) δ: 5.93 (1H, m, H-6), 5.76 (1H, m, H-7), 4.03–3.95 (1H, m, H-1′a), 3.81–3.76 (1H, t, $J_{1,2}$ = $J_{2,3}$ = 9.7 Hz, H-2), 3.61–3.52 (3H, m, H-1,3,4), 3.46–3.41 (1H, m, H-1′b), 2.54–2.47 (1H, m, H-8a), 2.22–2.15 (3H, m, H-5, H-9, H-10), 1.98–1.90 (1H, m, H-8b). ^{13}C NMR (125 MHz) δ: 128.3–127.2 (C-5, C-6, C arom.), 86.7 (C-1), 84.9 (C-2), 83.7 (C-3), 81.4 (C-4), 73.0 (C-1′), 40.0 (C-5), 38.2 (C-9), 33.7 (C-10), 31.2 ppm (C-8).

Anal. Calcd for $C_{46}H_{48}O_5$: C 81.2, H 7.1. Found: C 81.1, H 7.3%.

4.5. Epoxidation of 21

To a stirred and cooled to 4 °C solution of **21** (1.25 g, 1.84 mmol) in dichloromethane (20 mL), 55% 3-chloroperbenzoic acid (800 mg, 3.5 mmol) was added and the mixture was kept for 24 h at rt. The reaction was quenched with 2% aqueous NaOH (100 mL), the layers were separated, and the aqueous one extracted with CH_2Cl_2 (3x20 mL). Combined organic solutions were washed with brine,

dried, concentrated, and the residue was purified by column chromatography (hexane/EtOAc, 4:1) to afford a 1:1 mixture of **22** and **23** (0.86 g, 67%). *m*/*z* = 719.5 ([M+Na]$^+$). ^{1}H NMR (500 MHz) δ: 3.89–3.86 (H-1′), 3.79–3.75 (H-1′), 3.97–3.92, 3.73–3.65, 3.61–3.56, 3.46–3.38 (H-1, H-2, H-3, H-4), for **22**: 3.29 (H-6), 2.94 (H-7); for **23**: 3.39 (H-6), 3.33 (H-7), 3.26–3.22 (H-1′), 2.54–2.48, 2.25–2.10, 1.98–1.78, 1.67–1.55 ppm (H-5, H-8, H-9, H-10). ^{13}C NMR (125 MHz) δ: 87.1, 86.5, 83.7, 81.4, 79.9, 79.2 (C-1, C-2, C-3, C-4), 71.9 (C-1′), for **22**: 53.9 (C-7), 51.5 (C-6), for **23**: 53.7 (C-7), 53.0 (C-6), 38.9, 37.7, 32.9, 31.6, 30.06 (C-5, C-9, C-10), 31.0, and 27.7 ppm (C-8). Anal. Calcd for $C_{46}H_{48}O_6 + \frac{1}{4}H_2O$: C 78.8, H 7.0. Found: C 78.9, H 6.9%.

4.6. Isomerization of epoxides 22 and 23

To a solution of diphenyl diselenide (64 mg, 0.2 mmol) in anhydrous ethanol (5 mL), sodium borohydride (37 mg, 1.0 mmol) was added in portions under an argon atmosphere until the disappearance of the yellow color. After 5 min. a solution of a mixture of epoxides **22** and **23** (204 mg, 0.29 mmol) in anhydrous ethanol/THF (2 mL; 1:1 v/v) was added. The mixture was then heated at reflux for 2 h, then diluted with THF (10 mL), and cooled to 0 °C (ice-bath). Hydrogen peroxide (0.5 mL of a 30% solution in water, 4.4 mmol) was added dropwise, and the mixture was then allowed to warm to rt., and then kept at this temperature overnight. Saturated aqueous Na_2SO_4 (100 mL) and diethyl ether (20 mL) were added, the layers were separated and the aqueous phase extracted with diethyl ether (3 × 20 mL). The combined organic solutions were washed with saturated aqueous Na_2CO_3 (50 mL), dried, concentrated, and the products were isolated by column chromatography (hexane/EtOAc, 4:1–3:1) to afford **24** (68.7 mg, 32%) and **25** (43.5 mg, 20%) which were characterized as acetates.

4.6.1. (1*R*,2*R*,3*S*,4*R*,5*R*,6*R*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6-acetyloxy-9-benzyloxymethylbicyclo[4.4.0]dec-7,8-ene 24-Ac

$[\alpha]_D^{22} = -12.5$ (*c* 1, $CHCl_3$); *m*/*z* = 719.4 ([M+Na]$^+$). ^{1}H NMR (500 MHz) δ: 6.07 (1H, dd, $J_{7,8}$ = 10.0 Hz, $J_{8,9}$ = 2.3 Hz, H-8), 5.79–5.75 (1H, m, H-7), 5.43–5.40 (1H, dd, $J_{6,7}$ = 1.5 Hz, $J_{5,6}$ = 5.3 Hz, H-6), 4.41 (2H, m, H-1′, OC*H*$_2$Ph), 4.00 (1H, dd, $J_{9,1'}$ = 3.3 Hz, $J_{1',1'}$ = 8.7 Hz, H-1′), 3.80 (1H, t, $J_{1,2} = J_{2,3}$ = 9.5 Hz, H-2), 3.61–3.55 (2H, m, H-1,3), 3.55–3.51 (1H, m, H-1′), 3.39 (1H, dd, $J_{4,5}$ = 9.2 Hz, $J_{3,4}$ = 10.2 Hz, H-4), 2.58–2.52 (1H, m, H-10), 2.52–2.46 (1H, m, H-9), 1.99 (3H, s, C*H*$_3$CO), 1.88–1.84 ppm (1H, m, H-5). ^{13}C NMR (125 MHz) δ: 170.2 (CH$_3$*C*O), 138.7–138.6 (C-arom), 135.6 (C-8), 128.4–127.2 (C-arom), 122.4 (C-7), 86.4 (C-1), 83.9 (C-2), 82.5 (C-3), 78.3 (C-4), 72.91 (C-1′), 66.4 (C-6), 41.5 (C-5), 35.9 (C-9), 30.7 (C-10), 21.2 (*C*H$_3$CO). Anal. Calcd for $C_{48}H_{50}O_7$: C 78.0, H 6.8. Found: C 77.9, H 6.9%.

4.6.2. (1*R*,2*R*,3*S*,4*R*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-7-acetyloxy-9-benzyloxymethyl-bicyclo[4.4.0]dec-5,6-ene 25-Ac

$[\alpha]_D^{22} = -7.1$ (*c* 1, $CHCl_3$); *m*/*z* = 719.5 ([M+Na]$^+$). ^{1}H NMR (500 MHz) δ: 6.07 (1H, m, H-6), 5.33 (1H, m, H-7), 4.28 (1H, d, $J_{3,4}$ = 7.8 Hz, H-4), 3.82–3.77 (3H, m, H-1, H-2, H-3), 3.24–3.15 (2H, m, H-1′), 2.51–2.49 (1H, m, H-10), 2.22–2.14 (1H, m, H-9), 2.02 (3H, s, COC*H*$_3$), 2.01–1.95 (1H, m, H-8a), 1.73–1.66 ppm (1H, m, H-8b). ^{13}C NMR (125 MHz) δ: 170.7 (*C*H$_3$CO), 141.3 (C-5), 122.7 (C-6), 82.0 (C-1), 79.9 (C-2), 78.6 (C-4), 76.2 (C-3), 72.2 (C-1′), 66.7 (C-7), 37.9 (C-10), 31.5 (C-8), 30.9 (C-9), and 21.4 (*C*H$_3$CO).

Anal. Calcd for $C_{48}H_{50}O_7$: C 78.0, H 6.8. Found: C 77.8, H 6.9%.

4.7. The *cis*-dihydroxylation of 24-Ac

To a solution of **24-Ac** (54.1 mg, 73.2 μmol) in THF (4 mL), *t*-BuOH (0.4 mL), and water (0.05 mL), *N*-methylmorpholine-*N*-oxide (40 mg, 0.3 mmol) was added, followed by OsO_4 (2.5% solution in *t*-BuOH; 0.1 mL, 10 μmol) and the mixture was stirred for 5 days at rt (TLC monitoring in hexane/EtOAc, 2:1). Methanol (10 mL) was added followed by saturate aqueous $NaHSO_3$ (3 mL). The mixture was filtered through Celite, and the filtrate was partitioned between water (30 mL) and EtOAc (30 mL). The aqueous phase was extracted with EtOAc (3 × 30 mL), the combined organic solutions were washed with brine (40 mL), dried, and concentrated. Column chromatography (hexane/EtOAc 6:1–3:1) afforded product **26** (37 mg, 65%), which was characterized as a triacetate.

4.7.1. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*R*,8*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6,7,8-triacetyloxy-9-benzyloxymethylbicyclo[4.4.0]decane 26-(Ac)$_3$

$[\alpha]_D^{22} = -34.5$ = (c 1, CHCl3); m/z = 879.5 ([M+Na]+). ^{1}H NMR (600 MHz) δ: 5.49 (1H, dd, J5,6 = 2.0 Hz, J6,7 = 3.0 Hz, H-6), 5.39 (1H, dd, J7,8 = 3.6 Hz, H-7), 5.31 (1H, dd, J8,9 = 10.8 Hz, H-8), 4.09 (1H, d, J4,3 = 9.2 Hz, H-4), 4.07 (1H, d, J5′a,5′b = 9.0 Hz, H-5′a), 3.8 (1H, dd, J = 9.3 Hz, J = 10.3 Hz, H-2), 3.56–3.51 (2H, m, H-1, H-3), 3.48 (1H, dd, J4′,5′b = 2.6 Hz, H-5′b), 2.78–2.73 (1H, m, H-10), 2.14 (1H, m, H-9), 1.87 (1H, m, H-5), 2.12, 2,05, and 1.78 ppm (9H, 3 × s, 3 × CH3CO). ^{13}C NMR (150 MHz) δ: 169.7, 169.2, and 169.1 (3 × COCH3), 87.3 (C-1), 83.5 (C-3), 81.3 (C2), 78.0 (C-4), 69.4 (C-8), 68.9 (C-6, C-7), 65.1 (C-1′), 42.8 (C-5), 35.4 (C-9), 32.7 (C-10), 21.2, 21.1, and 20.7 ppm (3 × COCH3). Anal.: Calcd for C52H56O11 + ½H2O: C 72.1, H 6.63. Found: C 72.2, H 6.9%.

4.8. The *cis*-dihydroxylation of 11

Compound **11** (36.6 mg, 54 μmol) was dissolved in THF (4 mL) to which *t*-BuOH (0.4 mL), water (0.05 mL), and *N*-methyl-morpholine-*N*-oxide (40 mg, 0.3 mmol) were added, followed by OsO_4 (2.5% solution in *t*-BuOH; 0.1 mL, 10 μmol), and the mixture was stirred for 5 days at rt (TLC monitoring in hexane/EtOAc, 2:1). Methanol (10 mL) was then added followed by saturated aqueous $NaHSO_3$ (3 mL), the mixture was filtered through Celite, and the filtrate was partitioned between water (30 mL) and EtOAc (30 mL). The aqueous phase was extracted with EtOAc (3 × 30 mL), the combined organic layers were washed with brine (40 mL), dried, and concentrated. Column chromatography (hexane/EtOAc 6:1–3:1) afforded product **27** (26.6 mg, 60%), which was characterized as a triacetate.

4.8.1. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*R*,8*S*,9*S*,10*R*)-{1,2,3,4-Tetrabenzyloxy-6,7,8-triacetyloxy-9-[(4′*R*)-2′,2′-dimethyl-[1′,3′]-dioxolan-4′-yl]}bicyclo[4.4.0]decane 27-Ac$_3$

m/*z* = 859.7 ([M+Na]$^+$). ^{1}H NMR (600 MHz) δ: 5.62 (1H, dd, $J_{7,8}$ = 3.7 Hz, $J_{8,9}$ = 6.7 Hz, H-8), 5.43 (1H, m, H-6), 5.09 (1H, dd, $J_{6,7}$ = 6.5 Hz, H-7), 4.67–4.64 (1H, m, C-4′), 3.99–3.95 (1H, t, $J_{3,4} = J_{4,5}$ = 9.2 Hz, H-4), 3.95–3.91 (1H, t, *J* = 6.5 Hz, H-5a′), 3.87 (1H, t, *J* = 7.5 Hz, H-2), 3.67–3.61 (3H, m, H-5b,1,3), 2.45–2.41 (1H, m, H-5) 2.42–2.37 (1H, m, H-10), 2.18–2.13 (1H, m, H-9), 1.99–1.97 (6H, m, 2 × COC*H*$_3$), 1.94 (3H, s, COC*H*$_3$), 1.39–1.36 (3H, s, C(C*H*$_3$)$_2$), 1.27–1.24 ppm (3H, s, C(C*H*$_3$) $_2$). ^{13}C NMR (150 MHz) δ: 170, 169.5 and 169.5 (3 × *C*OCH$_3$), 108.5 (*C*(CH$_3$)$_2$), 85.9 (C-1), 81.7 (C-3), 81.3 (C-2), 78.6 (C-4), 75.4 (C-1′), 73.5 (C-7), 72.4 (C-8), 68.8 (C-6), 66.4 (C-2′), 43.2 (C-5), 39.9 (C-9), 34.1 (C-10), 26.2 and 25.2 (C(*C*H$_3$)$_2$), 21.1 and 20.8 ppm (3 × COC*H*$_3$).

4.9. Mitsunobu reaction of 12

(*This reaction was conducted under an argon atmosphere*) To a solution of **12** (21 mg, 30 μmol) in dry THF (5 mL), *p*-nitrobenzoic acid (16.8 mg, 0.1 mmol) and Ph_3P (26.3 mg, 0,1 mmol) were added followed by DIAD (20 mg, 0.1 mmol). The mixture was heated at reflux for 6 h, cooled to rt, and quenched with saturated aqueous $NaHCO_3$ (10 mL). Next it was partitioned between water

(30 mL) and EtOAc (20 mL), the organic phase was separated, and the aqueous one extracted with EtOAc (3 × 30 mL). The combined organic solutions were washed with brine (30 mL), dried, concentrated, and the residue was purified by column chromatography (hexane/EtOAc 5:1–2:1) to afford **28** (8 mg, 31%) and unreacted substrate **12** (13 mg, 62%).

4.9.1. (1*R*,2*R*,3*S*,4*R*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-9-benzyloxymethylbicyclo[4.4.0]-dec-5,6-en-7-yl 4-nitrobenzoate 28

$[\alpha]_D^{22} = +35.2$ (*c* 1, $CHCl_3$); *m*/*z* = 868.5 $[M+Na]^+$). ^1H NMR (600 MHz) *δ*: 6.01 (1H, s, H-6), 5.75 (1H, m, H-7), 4.21 (1H, d, $J_{3,4}$ = 6.6 Hz, H-4), 3.86–3.82 (1H, m, H-3), 3.76 (2H, m, H-1,2), 3.23–3.16 (2H, m, H-1′), 2.72–2.68 (1H, d, $J_{10,9}$ = 7.3 Hz, H-10), 2.36–2.35 (1H, m, H-8a), 2.26–2.24 (1H, m, H-9), 1.70–1.67 ppm (m, 1H, H-8b). ^{13}C NMR (150 MHz) *δ*: 164.3 [$OC(O)C_6H_4$-p-NO_2], 150.4 (C-5), 125.4 (C-6), 80.9 (C-3), 78.7 (C-4), 78.4 (C-2), 76,0 (C-1), 72.4 (C-1′), 72.0 (C-7), 37.1 (C-10), 33.8 (C-9), 31.7 (C-8). Anal.: Calcd for $C_{53}H_{51}O_9N$ + 1/2H_2O: C 74.5, H 6.1, N 1.6. Found: C 74.3, H 6.1, N 1.6%.

4.10. Mitsunobu reaction of 25

(*This reaction was conducted under an argon atmosphere*) To a solution of **25** (96.4 mg, 143 μmol) in dry THF (5 mL), *p*-nitrobenzoic acid (50.1 mg, 0.29 mmol), and Ph_3P (78.6 mg, 0.29 mmol) were added followed by DIAD (20 mg, 0.1 mmol). The mixture was heated at reflux for 4 h, cooled to rt., and quenched with saturated aqueous $NaHCO_3$ (10 mL). Next, it was partitioned between water (30 mL) and EtOAc (20 mL), the organic phase was separated, and the aqueous one extracted with EtOAc (3 × 30 mL). The combined organic solutions were washed with brine (30 mL), dried, concentrated, and the residue was purified by column chromatography (hexane/EtOAc 5:1–2:1) to afford **29** (30 mg, 25%) and unreacted substrate **25** (58 mg, 60%).

4.10.1. (1*R*,2*R*,3*S*,4*R*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-9-[(4′*R*)-2′,2′-dimethyl-1′,3′-dioxolan-4′-yl]bicyclo[4.4.0]-dec-5,6-en-7-yl 4-nitrobenzoate 29

$[\alpha]_D^{22} = +80.7$ (*c* 1, $CHCl_3$); *m*/*z* = 848.5 ($[M+Na]^+$). ^1H NMR (600 MHz) *δ*: 6.01 (1H, s, H-6), 5.71 (1H, m, H-7), 4.17 (1H, d, $J_{3,4}$ = 6.4 Hz, H-4), 4.06 (1H, m, H-1), 3.95–3.1 (2H, m, H-4′,5′), 3.83–3.81 (1H, dd, $J_{2,3}$ = 4.1 Hz, H-3), 3.76–3.72 (1H, dd, $J_{1,2}$ = 1.9 Hz, H-2), 3.56–3.52 (1H, m, H-5′), 2.72–2.69 (1H, m, H-10), 2.28–2.22 (1H, m, H-9), 2.20–2.17 (1H, m, H-8a), 1.47–1.42 (1H, m, H-8b), 1.36 and 1.25 ppm (3H, 2 × s, $C(CH_3)_2$). ^{13}C NMR (150 MHz) *δ*: 164.2 [$OC(O)C_6H_4$-4-NO_2], 150.5 (C-5), 109.0 ($C(CH_3)_2$), 71.3 (C-7), 125.9 (C-6), 80.6 (C-3), 78.7 (C-4), 78.4 (C-4′), 77.8 (C-2), 77.1 (C-2), 67.6 (C-5′), 38.1 (C-10), 35.9 (C-9), 29.5 (C-8), 26.7, and 25.7 ppm ($C(CH_3)_2$). Anal. Calcd for $C_{50}H_{51}O_{10}N$ + 2H_2O: C 69.67, H 6.43, N 1.62. Found: C 69.4, H 6.21, N 1.94.

4.11. Reaction of oxiranes 9 and 10 with HSCN

General procedure: An ether solution of HSCN was prepared according to the literature.[24] Six drops of concentrated *ortho*-phosphoric acid were added to a saturated aqueous solution of KSCN (20 mL) and the in situ formed HSCN was extracted with diethyl ether (10 mL), providing a crude pink solution, which was used directly in the next step.

This mixture was added to a stirred and cooled (0 °C) solution of the epoxide (140 mg, 0.21 mmol) in ether (20 mL), containing small amounts of hydroquinone as stabilizer, until the solution became pink. The cooling bath was removed and the solution was kept overnight at room temp. TLC analysis (hexane/ethyl acetate, 3:1) indicated the disappearance of the starting material and the formation of a new slightly more polar product. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL) and partitioned between ethyl acetate (20 mL) and water (20 mL). The organic layer was separated, and the aqueous one extracted with EtOAc (2 × 20 mL). The combined organic solutions were washed with water (15 mL) and brine (15 ml), dried, concentrated, and the product was isolated by column chromatography (hexane/ethyl acetate, 4:1–3:1) to afford thiocyanate **31** (from **10**; 106.5 mg, 71%) or **30** (from **9**; 143.5 mg, 93%) as amorphous solids. These compounds were characterized as acetates.

4.11.1. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6-acetyloxy-7-thiocyano-9-[(4′*R*)-2′,2′-dimethyl-1′,3′-dioxolan-4′-ylo]bicyclo[4.4.0]decane 30-Ac

$[\alpha]_D^{22} = +16.6$ (*c* 1, $CHCl_3$); *m*/*z*: 800.3193; Calcd for $C_{46}H_{51}NO_8S$-Na ($M+Na^+$): 800.3228. IR ($CHCl_3$ film) *ν*: 2153 (SCN), 1741, 1454, 1370, 1225, 1069, 736, 698 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6, 80 °C) *δ*: 5.55 (1H, app. t, H-6, *J* = 10.0 Hz), 4.68–4.46 (8H, m, OCH_2Ph), 4.31 (1H, app. dd, H-1′, *J* = 14.2, 6.7 Hz), 4.00 (1H, dd, H-2′a, *J* = 7.9, 6.5 Hz), 3.78 (1H, m, H-2), 3.71 (4H, m, H-1, H-3, H-4, H-7), 3.53 (1H, m, H-2′b), 2.61 (1H, m, H-10), 2.38 (2H, m, H-5, H-8a), 1.90 (3H, s, CH_3CO), 1.84 (2H, m, H-8b, H-9), 1.30 and 1.27 ppm (2 × s, 6H, $(CH_3)_2C$). ^{13}C NMR (150 MHz, DMSO-d_6, 80 °C) *δ*: 169.2 (CH_3CO), 110.5 (SCN), 108.0 (C-4′), 81.7 (C-1), 79.2 (C-3), 77.9 (C-2), 76.3 (C-4), 75.8 (C-1′), 73.8 (C-6), 67.0 (C-2′), 49.2 (C-7), 41.2 (C-5), 40.0 (C-9) 31.9 (C-10), 31.6 (C-8), 26.2 and 25.0 ($(CH_3)_2C$), 20.0 ppm (CH_3CO).

4.11.2. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6-thiocyano-7-acetyloxy-9-[(4′*R*)-2′,2′-dimethyl-1′,3′-dioxolan-4′-yl]bicyclo[4.4.0]decane 31-Ac

$[\alpha]_D^{22} = -1.4$ (*c* 1, $CHCl_3$); *m*/*z*: 800.3190; Calcd for $C_{46}H_{51}NO_8S$ ($M+Na^+$): 800.3228. IR ($CHCl_3$ film) *ν*: 2152 (SCN), 1742, 1454, 1370, 1230, 1068, 736, 698 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6, 80 °C) *δ*: 5.04 (td, 1H, H-7, *J* = 8.6, 5.0 Hz), 4.65–4.51 (m, 8H, OCH_2Ph), 4.30 (dd, 1H, H-1′, *J* = 13.4, 6.6 Hz), 4.10 (m, 1H, H-4), 4.06 (m, 1H, H-6), 3.90 (m, 2H, H-2, H-2′a), 3.80 (app. t, 1H, H-3, *J* = 5.3 Hz), 3.74 (app. t, 1H, H-1, *J* = 3.4 Hz), 3.54 (dd, 1H, H-2′b), 2.57 (m, 1H, H-10), 2.36 (app. dt, 1H, H-5, *J* = 10.4, 5.4 Hz), 2.15 (ddd, 1H, H-8a, *J* = 14.0, 8.8, 5.4 Hz), 2.02 (m, 1H, H-9), 2.00 (s, 3H, CH_3CO), 1.69 (app. dt, 1H, H-8b, *J* = 13.6, 5.0 Hz), 1.29 and 1.23 ppm (2 × s, 6H, $(CH_3)_2C$). ^{13}C NMR (150 MHz, DMSO-d_6, 80 °C) *δ*: 168.8 (CH_3CO), 110.2 (SCN), 107.9 (C-4′), 81.3 (C-1), 79.0 (C-3), 76.5 (C-2), 76.3 (C-4), 75.9 (C-1′), 71.7 (C-7), 66.3 (C-2′), 51.4 (C-6), 39.1 (C-5), 37.2 (C-9), 32.7 (C-10), 29.5 (C-8), 26.2 and 25.0 ($(CH_3)_2C$), 20.2 ppm ($CH_3C(O)$).

4.12. Reaction of oxiranes 9 and 10 with the phosphide anion

General procedure: To a stirred solution of epoxide **9** or **10** (50 mg, 0.073 mmol) in dry THF (30 mL, distilled over sodium prior to use), under an argon atmosphere, potassium diphenylphosphide [Ph_2PK; 0.37 ml of a 0.5 M solution in THF] was added at room temperature. After 40 min., the solution changed color from orange to pale yellow and TLC analysis (hexane/ethyl acetate, 3:1) indicated the disappearance of the starting material. The crude reaction mixture (composed of the phosphine and phosphine oxide) was exposed to air; after 1.5 h TLC confirmed the full conversion of the phosphine into the phosphine oxide. The mixture was partitioned between water (50 mL) and ethyl acetate (30 mL); the organic layer was separated, and the aqueous one extracted with EtOAc (2 × 30 mL). The combined organic solutions were washed with water (15 mL) and brine (15 ml), dried, concentrated, and the product was isolated by column chromatography (hexane/ethyl acetate, 3:1) to afford **33** (from **10**; 59 mg, 92%) or **32** (from **9**; 42 mg, 71%) as amorphous solids. Compound **32** was characterized as an acetate.

4.12.1. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6-acetyloxy-7-diphenylphosphoryl-9-[(4′*R*)-2′,2′-dimethyl-1′,3′-dioxolan-4′-yl]bicyclo[4.4.0]-decane 32-Ac

$[\alpha]_D^{26} = -1.7$ (*c* 1, $CHCl_3$); *m*/*z*: 943.3973; Calcd for $C_{57}H_{61}O_9PNa$ ($M+Na^+$): 943.3945. ^1H NMR (600 MHz, DMSO-d_6, 80 °C) δ: 5.76 (m, 1H, H-6), 4.79–4.48 (8H, OCH_2Ph), 4.55 (m, 1H, H-1′), 4.29 (app. t, 1H, H-4, *J* = 8.7 Hz), 4.04 (dd, 1H, H-2, *J* = 14.2, 7.1 Hz), 3.68 (app. t, 1H, H-2′a, *J* = 7.5 Hz), 3.62 (app. t, 1H, H-1, *J* = 7.4 Hz), 3.58 (m, 1H, H-3), 3.42 (m, 1H, H-2′b), 3.11 (m, 1H, H-7), 2.27 (m, 1H, H-10), 2.22 (m, 1H, H-9), 2.13 (m, 1H, H-5), 2.02 (m, 1H, H-8a), 1.52 (s, 3H, CH_3C(O)), 1.41 (m, 1H, H-8b), 1.19 and 1.01 ppm (2 × s, 6H, $(CH_3)_2$C); ^{13}C NMR (150 MHz, DMSO-d_6, 80 °C) δ: 168.3 (CH_3C(O)), 107.1 (C-4′), 84.7 (C-3), 82.3 (C-1), 80.8 (C-2), 76.3 (C-4), 75.3 (C-1′), 68.8 (C-5), 64.5 (C-2′), 43.0 (C-5), 36.6 and 36.1 (d, C-7, J_{CP} = 69 Hz), 35.2 (C-9 and C-10), 25.4 and 24.4 ((CH_3)$_2$C), 21.1 (C-8), 20.0 ppm (CH_3C(O)). ^{31}P NMR (243 MHz, DMSO-d_6, 80 °C) δ: 31.4 ppm.

4.12.2. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6-diphenylphosphoryl-7-hydroxy-9-[(4′*R*)-2′,2′-dimethyl-1′,3′-dioxolan-4′-yl]bicyclo-[4.4.0]decane 33

$[\alpha]_D^{22} = -1.4$ (c 1, CHCl3); m/z: 901.3818; Calcd for C55H59O8P-Na (M+Na+): 901.3840. ^1H NMR (600 MHz, C6D6, 25 °C) δ: 5.32 (app. dd, 1H, H-1′), 5.22–4.48 (9H, m, OCH2Ph, H-4), 4.36 (1H, H-7), 4.30 (m, 2H, H-2′a, OCH2Ph), 4,09 (dd, 1H, H-2′b, J = 8.4, 7.3 Hz), 3,88 (dd, 1H, H-2, J = 10.4, 9.2 Hz), 3.50 (app. d, 1H, H-6, J = 11.8 Hz), 3,24 (m, 2H, H-1, H-3), 2.97 (dt, 1H, H-10, J = 12.3, 4.1 Hz), 2.74 (m, 1H, H-9), 2.38 (m, 1H, H-8a), 2.28 (1H, m, H-8b), 2.17 (m, 1H, H-5), 1.51 and 1.35 ppm (2 × s, 6H, $(CH_3)_2^m$, C). ^{13}C NMR (150 MHz, C6D6, 25 °C) δ: 107.9 (C-4′), 88.2 (C-3), 84.0 (C-1), 82.2 (C-2, C-4), 75.6 (C-1′), 66.2 (C-7), 64.6 (C-2′), 39.2 (C-10), 38.7 (C-5), 38.4 and 37.9 (d, C-6, JCP = 69 Hz), 31.7 (C-8), 31.2 (C-9), 26.3 and 24.5 ppm ((CH3)2C). 31P NMR (243 MHz, C6D6) δ: 32.6 ppm.

4.13. Reduction of the thiocyanates 30 and 31 with $LiAlH_4$

General procedure: (*This reaction was performed under an argon atmosphere*): To a stirred solution of the thiocyanate (37 mg, 0.05 mmol) in dry THF (3 mL), a solution of $LiAlH_4$ (8 mg) in THF (2 mL) was added. After 5 min. TLC analysis (hexane/ethyl acetate, 3:1) showed the disappearance of the starting material and the formation of a new, slightly less polar product. The reaction was quenched with water (1 mL) and partitioned between water (10 mL) and ethyl acetate (15 mL). The phases were separated and the aqueous one extracted with ethyl acetate (2 × 15 mL). The combined organic solutions were washed with brine (5 mL), dried, and concentrated, and the crude product was purified via preparative TLC (hexane-ethyl acetate, 2:1) to afford a pale yellow, amorphous solid: **34** (24.7 mg, 69%) or **35** (24 mg, 67%).

4.13.1. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6-hydroxy-7-sulfanyl-9-[(4′*R*)-2′,2′-dimethyl-1′,3′-dioxolan-4′-ylo]bicyclo[4.4.0]decane 34

$[\alpha]_D^{22} = +20.5$ (*c* 1, $CHCl_3$); *m*/*z*: 733.3169, Calcd for $C_{43}H_{50}O_7SNa$ ($M+Na^+$): 733.3170. ^1H NMR (600 MHz, DMSO-d_6, 80 °C) δ: 4.67–4.50 (m, 7H, OCH_2Ph), 4.47 (d, 1H, O*H*, *J* = 6.3 Hz), 4.32 (app. dd, 1H, H-1′, *J* = 14.1, 6.8 Hz), 4.02 (m, 1H, H-4), 3.92 (dd, 1H, H-2′a, *J* = 8.0, 6.3 Hz), 3.80 (m, 1H, H-6), 3.77 (m, 1H, H-2), 3.67 (app. t, 1H, H-3, *J* = 6.6 Hz), 3.62 (app. t, 1H, H-1, *J* = 3.9 Hz), 3.52 (m, 1H, H-2′b), 3.49 (dd, 1H, H-1, *J* = 8.1, 6.9 Hz), 2.97 (ddd, 1H, H-7, *J* = 12.4, 9.9, 4.5 Hz), 2.51 (m, 1H, H-10), 2.19 (d, 1H, S*H*, *J* = 4.6 Hz), 2.08 (m, 1H, H-8a), 1.97 (m, 1H, H-5), 1.84 (app. td, 1H, H-9, *J* = 8.8, 4.6 Hz), 1.62 (app. dt, 1H, H-8b, *J* = 13.7, 4.4 Hz), 1.29 and 1.23 ppm (2 × s, 6H, $(CH_3)_2$C). ^{13}C NMR (150 MHz, DMSO-d_6, 80 °C) δ: 107.5 (C-4′), 83.0 (C-1), 81.5 (C-3), 79.1 (C-2), 77.9 (C-4), 75.7 (C-1′), 73.4 (C-6), 66.6 (C-2′), 44.0 (C-5), 41.6 (C-7), 40.8 (C-10), 38.4 (C-9), 33.2 (C-8), 26.2 and 25.0 ppm ((CH_3)$_2$C).

4.13.2. (1*R*,2*R*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-1,2,3,4-Tetrabenzyloxy-6-sulfanyl-7-hydroxy-9-[(4′*R*)-2′,2′-dimethyl-1′,3′-dioxolan-4′-ylo]bicyclo[4.4.0]decane 35

$[\alpha]_D^{19} = +14.5$ (*c* 1, $CHCl_3$); *m*/*z*: 733.3201, Calcd for $C_{43}H_{50}O_7SNa$ ($M+Na^+$): 733.3170. ^1H NMR (600 MHz, DMSO-d_6, 80 °C) δ: 4.98 (m, 1H, O*H*), 4.74–4.61 (m, 9H, OCH_2Ph, H-1′), 4.26 (m, 1H, H-4), 3.82 (m, 1H, H-7), 3.79 (m, 1H, H-2), 3.68 (dd, 1H, H-2′a, *J* = 8.0, 7.0 Hz), 3.62 (m, 1H, H-2′b), 3.55 (m, 1H, H-6), 3.49 (m, 1H, H-1), 3.44 (m, 1H, H-3), 2.63 (d, 1H, S*H*, *J* = 7.2 Hz), 2.25 (m, 2H, H-9, H-10), 1.86 (m, 2H, H-5, H-8a), 1.61 (m, 1H, H-8b), 1.31 and 1.18 ppm (2 × s, 6H, $(CH_3)_2$C). ^{13}C NMR (150 MHz, DMSO-d_6,

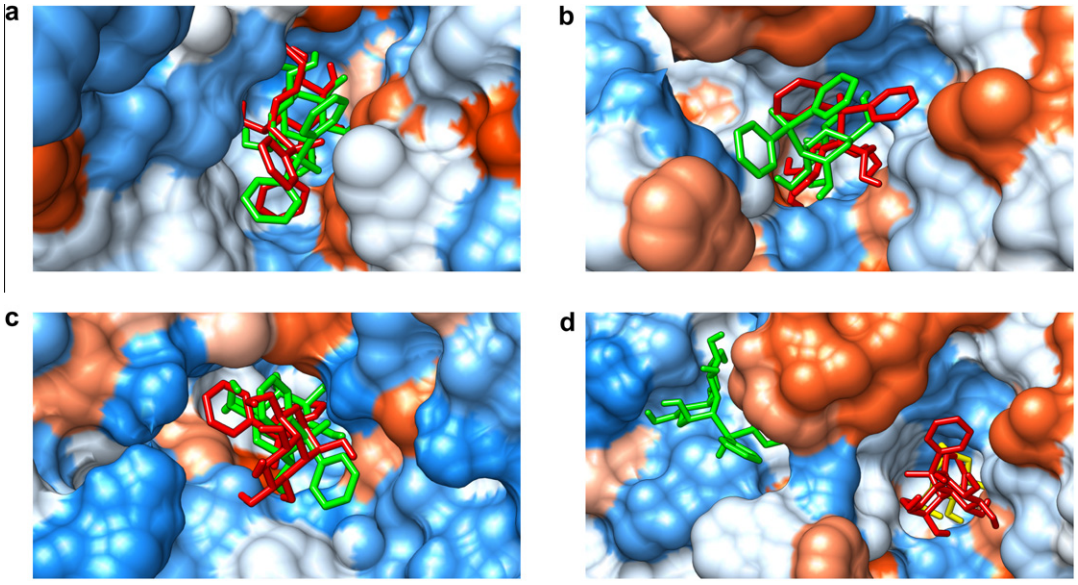


Figure 10. The lowest energy binding poses for (red: AD4.2, green: Vina): (a) **32a** in 1U33; (b) **33a** in 2NSX; (c) **32a** in 1FO3; and (d) **33a** in 3GXF (yellow: ligand/isofagomine). The hydrophobicity surface of the receptor is shown.

80 °C) δ: 106.8 (C-4′), 85.4 (C-3), 83.0 (C-1), 80.3 (C-2), 79.3 (C-4), 74.7 (C-1′), 70.7 (C-7), 63.8 (C-2′), 45.0 (C-5), 40.3 (C-6), 35.1 (C-9) 32.2 (C-10), 27.3 (C-8), 25.6 and 24.1 ((CH_3)$_2$C), 20.1 ppm (C-8).

4.14. Molecular docking

The potential inhibitory activities of the obtained compounds were examined by using AutoDock 4.2 and AutoDock Vina. AutoDock Tools 1.5.4 was used to prepare docking input files and to evaluate the results. In order to prepare a receptor for docking, all small molecules, ions, and ligands were removed, then, polar hydrogen atoms were added, whereas the non-polar ones were merged. Gasteiger charges were computed. The B3LYP/6-31G(d) geometry optimization (Gaussian03) of **27a**, **32a**, **33a**, **34a**, and **35a** allowed us to find the lowest-energy conformers (those shown in the Fig. 10). Subsequently, partial charges and polar hydrogen atoms were added to them.

In case of Autodock 4.2, AutoGrid was launched prior to docking, using a grid box 60–60–60 with a spacing of 0.375 Å, centered at the position of the initial PDB ligand. For docking, the Lamarckian GA-LS was used (number of runs: 250, population size: 250, RMSD tolerance for cluster analysis: 3 Å, other parameters kept default). Whenever several clusters were obtained, the docking was redone with the number of runs reduced to 100, and the number of energy evaluation number increased to 25×10^6. The first two changes significantly reduced the process time, whereas the latter gave a better result convergence.

When AutoDock Vina was employed, all docking parameters were kept default except for 'exhaustiveness' (set to 10). The grid box 30–30–30 with (default) spacing of 1 Å was used. The results were visualized with Chimera 1.6rc.[32]

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References

1. (a) Robina, I.; Moreno-Vargas, A. J.; Carmona, A. T.; Vogel, P. *Curr. Drug Metab.* **2004**, *5*, 329–361; (b) Ganem, B. Glycomimetics that Inhibit Carbohydrate Metabolites. In *Carbohydrate Mimics. Concepts and Methods*; Chapleur, Y., Ed.; Wiley: Weinheim, 1998; pp 239–258; (c) Tatsuta, K. Total Synthesis and Chemical Design of Useful Glycosidase Inhibitors. In *Carbohydrate Mimics. Concepts and Methods*; Chapleur, Y., Ed.; Wiley: Weinheim, 1998; pp 283–306.
2. (a) Davies, B. G. *Tetrahedron: Asymmetry* **2009**, *20*, 652–671; (b)Stütz, A., Ed.Iminosugars as Glycosidases Inhibitors: Norjirmycin and Beyond; Wiley-VCH: Weinheim, 1999; (c) Compain, P.; Martin, O. R. *Iminosugars: From Synthesis to Therapeutic Applications*; John Wiley and Sons: Chichester, 2007.
3. (a) Legler, G. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 319–384; (b) Billington, D. C.; Perron-Sierra, F.; Picard, L.; Beaubras, S.; Duhault, J.; Espinal, J.; Challal, S. Conduritols and Analogues as Insulin Modulators. In *Carbohydrate Mimics. Concepts and Methods*; Chapleur, Yves, Ed.; Wiley-VCH: Weinheim, 1998; pp 433–442; (c) Gültekin, M. S.; Çelik, M.; Balci, M. *Curr. Org. Chem.* **2004**, *8*, 1159–1186.
4. (a) Marco-Contelles, J. *Eur. J. Org. Chem.* **2001**, 1607–1618; (b) Gloster, T. M.; Madsen, R.; Davies, G. J. *Org. Biomol. Chem.* **2007**, *5*, 444–446.
5. (a) Berridge, M. J.; Irvine, R. F. *Nature* **1989**, *341*, 197–205; (b) Berridge, M. J. *Nature* **1993**, *361*, 315–325; (c) Hinterding, K.; Dıaz, D. A.; Waldmann, H. *Angew. Chem., Int. Ed.* **1998**, *37*, 688–749; (d) Kilbas, B.; Balci, M. *Tetrahedron Lett.* **2011**, *67*, 2355–2389.
6. (a) Arjona, O.; Gomez, A. M.; Lopez, J. C.; Plumet, J. *Chem. Rev.* **2007**, *107*, 1919–2036; (b) Kobayashi, Y. Carbasugars: Synthesis and Functions. In *Glycoscience*; Fraser-Reid, B., Tatsuta, K., Eds.; Springer: Berlin, Heidelberg, 2008; pp 1915–1998.
7. (a) Mehta, G.; Ramesh, S. S. *Chem. Commun.* **2000**, 2429–2430; (b) Mehta, G.; Ramesh, S. S. *Tetrahedron Lett.* **2001**, *42*, 1987–1990; (c) Mehta, G.; Ramesh, S. S. *Can. J. Chem.* **2005**, *83*, 581–594.
8. Mehta, G.; Reddy, D. S.; Ramesh, S. S.; Tatu, U. *Tetrahedron Lett.* **1999**, *40*, 9141–9144.
9. Kallmerten, J. The Chemistry of the Nargenicin Macrolides. In: *Studies in Natural Product Chemistry, Structure and Chemistry (Part D)*; Atta-ur-Rahman, Ed.; Elsevier; Vol. 17, pp 288–311.
10. (a) Roush, W. R.; Koyama, K.; Curtin, M. L.; Moriarty, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 7502–7512; (b) Coe, J. W.; Roush, W. R. *J. Org. Chem.* **1989**, *54*, 915–930.
11. (a) Enev, V. S.; Drescher, M.; Kaehling, H.; Mulzer, J. *Synlett* **2005**, 2227–2229; (b) Felzmann, W.; Arion, V. B.; Mieusset, J. L.; Mulzer, J. *Org. Lett.* **2006**, *8*, 3849–3851; (c) Marchart, S.; Mulzer, J.; Enev, V. S. *Org. Lett.* **2007**, *9*, 813–816.
12. (a) Kara, Y.; Balci, M. *Tetrahedron Lett.* **2003**, *59*, 2063–2066; (b) Baran, A.; Balci, M. *J. Org. Chem.* **2008**, *73*, 4370–4375.
13. Castanospermine analogues: (a) Michael, J. P. *Nat. Prod. Rep.* **1998**, *5*, 571–594; Quinolizidine analogues: (b) Liu, P. S.; Rogers, R. S.; Kang, M. S.; Sunkara, P. S. *Tetrahedron Lett.* **1991**, *42*, 5853–5856; (c) Bell, A. A.; Pickering, L.; Watson, A. A.; Nash, R. J.; Griffiths, R. C.; Jones, M. G.; Fleet, G. W. J. *Tetrahedron Lett.* **1996**, *47*, 8561–8564; (d) Yoda, H.; Nakajima, T.; Takabe, K. *Synlett* **1997**, 911–912; (e) Herczegh, P.; Kovacs, I.; Szilagyi, L.; Sztaricskai, F.; Berecibar, A.; Riche, C.; Chiaroni, A.; Olesker, A.; Lukacs, G. *Tetrahedron Lett.* **1995**, *51*, 2969–2978; (f) Pearson, W. H.; Hembre, E. J. *J. Org. Chem.* **1996**, *61*, 5537–5545.
14. (a) Chou, T.-C.; Chiou, J. H. *J. Chin. Chem. Soc. (Tapei)* **1986**, *33*, 227–234; (b) Forman, M. A.; Dailey, W. P. *J. Org. Chem.* **1993**, *58*, 1501–1507; (c) Mehta, G.; Pallavi, K. *Chem. Commun.* **2002**, 2828–2829; (d) Mehta, G.; Ramesh, S. S.; Bera, M. K. *Chem. Eur. J.* **2003**, *9*, 2264–2272; (e) Mehta, G.; Ramesh, S. S. *Tetrahedron Lett.* **2003**, *44*, 3105–3108; (f) Mehta, G.; Pallavi, K. *Tetrahedron Lett.* **2004**, *45*, 3865–3867; (g) Mehta, G.; Ramesh, S. S.; Sen, S. *Proc. Indian Natl. Sci. Acad.* **2005**, *71A*, 121; (h) Mehta, G.; Ramesh, S. S.; Sen, S. *CrystEngComm* **2005**, *7*, 656–663; (i) Mehta, G.; Pujar, S. R.; Ramesh, S. S.; Islam, K. *Tetrahedron Lett.* **2005**, *46*, 3373–3376; (j) Mehta, G.; Sen, S.; Venkatesan, K. *CrystEngComm* **2007**, *9*, 144–151; (k) Nowogródzki, M.; Jarosz, S. *Curr. Org. Chem.* **2010**, *14*, 533–545.
15. Mehta, G.; Reddy, D. S. *Tetrahedron Lett.* **1999**, *40*, 991–994.
16. (a) Herczegh, P.; Zsely, M.; Szilagyi, L.; Bognar, R. *Tetrahedron Lett.* **1988**, *29*, 481–484; (b) Herczegh, P.; Zsely, M.; Szilagyi, L.; Dinya, Z.; Bognar, R. *Tetrahedron Lett.* **1989**, *45*, 5995–6002; (c) Herczegh, P.; Zsély, M.; Szilágyi, L.; Bajza, I.; Kovács, Á.; Batta, G.; Bognár, R. *Cycloaddition Reactions in Carbohydrate Chemistry*; ACS Symposium Series, 1992; Vol. 494, Chapter 8, pp 112–130.
17. Review: (a) Jarosz, S. *Curr. Org. Chem.* **2008**, *12*, 985–994; Microreview: (b) Jarosz, S.; Gaweł, A. *Eur. J. Org. Chem.* **2005**, 3415–3432.
18. (a) Jarosz, S.; Skóra, S. *Tetrahedron: Asymmetry* **2000**, *11*, 1425–1432; (b) Jarosz, S.; Szewczyk, K.; Zawisza, A. *Tetrahedron: Asymmetry* **2003**, *14*, 1709–1713.
19. Nowogródzki, M.; Jarosz, S. *Curr. Org. Chem.* **2010**, *14*, 601–613.
20. Jarosz, S.; Skóra, S. *Tetrahedron: Asymmetry* **2000**, *11*, 1433–1448.
21. Jarosz, S.; Skóra, S. *Tetrahedron: Asymmetry* **2001**, *12*, 1651–1656.
22. (a) Jarosz, S.; Nowogródzki, M. *J. Carbohydr. Chem.* **2006**, *25*, 139–149; (b) Jarosz, S.; Nowogródzki, M.; Kołaczek, M. *Tetrahedron: Asymmetry* **2007**, *18*, 2674–2679.
23. Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3943–3946.
24. Price, C. C.; Kirk, P. F. *J. Am. Chem. Soc.* **1953**, *75*, 2396–2400.
25. Vedejs, E.; Snoble, K. A. J.; Fuchs, Ph. L. *J. Org. Chem.* **1973**, *38*, 1178–1183.
26. Such facile oxidation of a phosphine even under an argon atmosphere was previously observed by us: Gaweł, A.; Jarosz, S. *J. Carbohydr. Chem.* **2010**, *29*, 332–347.
27. Fürst, A.; Plattner, P. A. *Helv. Chim. Acta* **1949**, *32*, 275–283.
28. (a) Pakulski, Z.; Pierożyński, D.; Zamojski, A. *Tetrahedron Lett.* **1994**, *50*, 2975–2992; (b) Adams, R.; Bramlet, H. B.; Tendick, F. H. *J. Am. Chem. Soc.* **1920**, *42*, 2369–2374.
29. Morris, G. M.; Huey, R.; Lindstrom, W.; Sanner, M. F.; Belew, R. K.; Goodsell, D. S.; Olson, A. J. *J. Comput. Chem.* **2009**, *30*, 2785–2791.
30. Trott, O.; Olson, A. J. *J. Comput. Chem.* **2010**, *31*, 455–461.
31. Daumas, M.; Vo-Quang, Y.; Vo-Quang, L.; Le Goffic, F. *Synthesis* **1989**, 64–65.
32. Pettersen, E. F.; Goddard, T. D.; Huang, C. C.; Couch, G. S.; Greenblatt, D. M.; Meng, E. C.; Ferrin, T. E. *J. Comput. Chem.* **2004**, *25*, 1605–1612.