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Synthesis of amino-1,4-anhydro-D-pentitols and amino-1,5-anhydro-D-hexitols with the *arabino* configuration from (*R*)-glycidol

Sílvia Aragonès, Fernando Bravo,* Yolanda Díaz, Mª Isabel Matheu and Sergio Castillón*

Departament de Química Analítica i Química Orgànica, Facultat de Química, Universitat Rovira i Virgili, Pl. Imperial Tarraco 1, 43005 Tarragona, Spain

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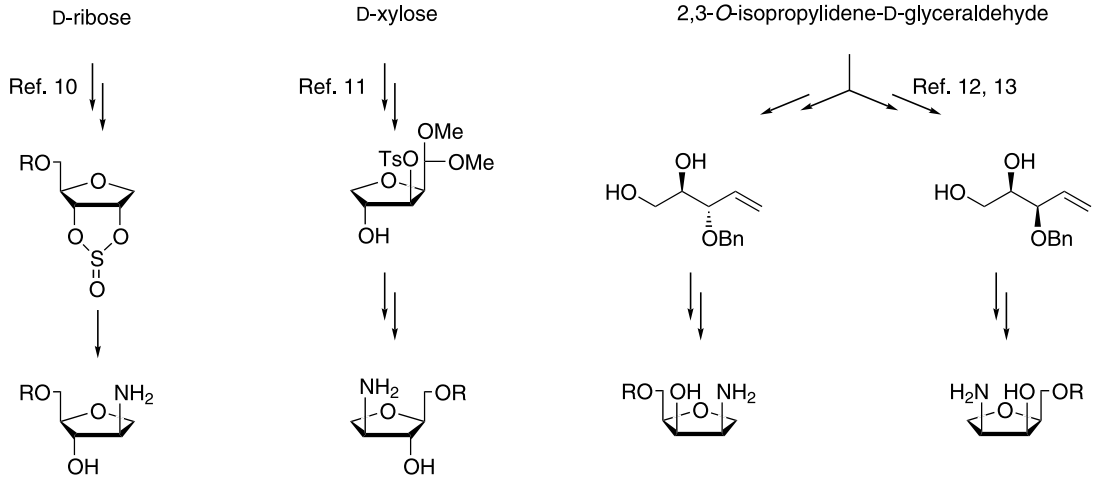
Abstract—2-Amino-1,4-anhydro-pentitol and 3-amino-1,5-anhydro-4-deoxy-hexitol with the *arabino* configuration were synthesised from (*R*)-glycidol using a metathesis reaction as the key step. The dihydrofuran or dihydropyran products obtained after the metathesis reaction were subjected to epoxidation, epoxide opening with azide anion and finally azide reduction.

1. Introduction

Enantiomerically pure amino-anhydro-alditols are a class of compounds used as monosaccharide mimetic structures and amino acid surrogates,[1] as well as precursors of several organic molecules. In this sense, they have been used as key intermediates in the synthesis of some natural products,[2] protease inhibitors[3–5] and isonucleosides,[6–9] among other examples. In particular, D- and L-enantiomers of 2-amino-1,4-anhydro-*arabino*-pentitol have been prepared from D-ribose[10] and D-xylose[11] (Scheme 1), respectively, and used in the synthesis of D- and L-isonucleosides. We recently described a method for preparing both enantiomers of 2-amino-1,4-anhydro-pentitol with the *lyxo* configuration and their corresponding purine and pyrimidine isonucleosides from D-glyceraldehyde (Scheme 1),[12] using a iodocycloetherification reaction as the key



Scheme 1.

* Corresponding authors. E-mail: castillon@quimica.urv.es

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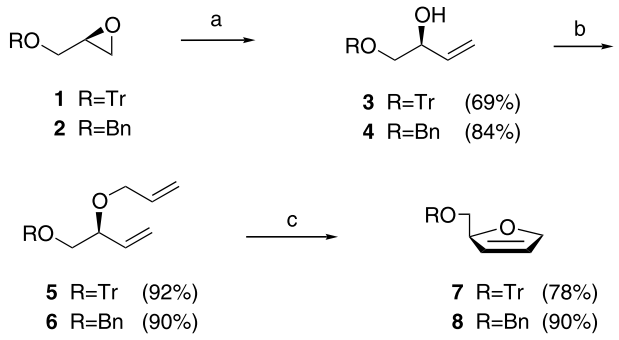
step.[13] In relation to our previous work, we describe herein an alternative procedure for synthesising 2-amino-1,4-anhydro-*arabino*-pentitol from glycidol. Both enantiomers can be synthesised by selecting the configuration of the starting glycidol. In addition, we have also explored the synthesis of amino-1,5-anhydro-4-deoxy-*arabino*-hexitols.

2. Results and discussion

As Scheme 2 shows, glycidol can serve as the starting material for synthesising 2-amino-1,4-anhydro-*arabino*-pentitol. A useful approach to the synthesis of aminoalditols with amino and hydroxyl groups in a *trans* disposition is to open an epoxide with an azide ion. This epoxide could be formed from a chiral dihydrofuran. We recently reported the synthesis of homochiral dihydrofurans based on a regioselective selenoxide elimination (Scheme 2).[14] On the other hand, the metathesis reaction has emerged as an outstanding procedure for synthesising medium and large cycles. Therefore, we considered that the metathesis reaction from an appropriate diene, which can easily be prepared from (*R*)-glycidol, would be appropriate for synthesising dihydrofurans.

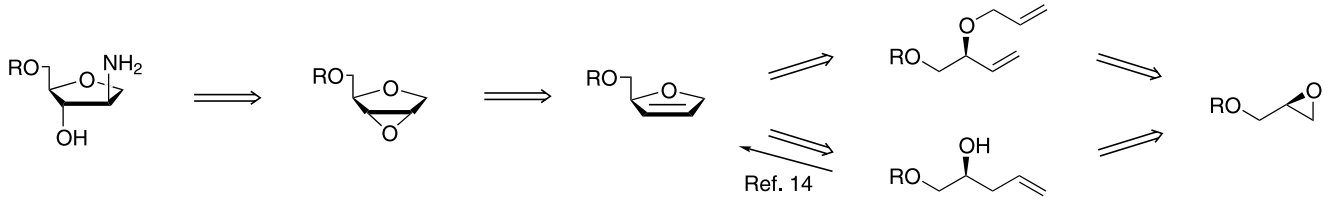
With the aim of exploring how the protecting group affects the stereoselectivity of the epoxidation reaction, we protected (*R*)-glycidol as the trityl and benzyl ethers **1** and **2** (Scheme 3). Opening these epoxides with the in situ generated sulfur ylide $CH_2{=}SMe_2$[15] resulted in the formation of butenols **3** and **4**[16] (69 and 84% yields, respectively). The secondary alcohol was then protected with allyl bromide, to obtain the metathesis precursors **5** (92%) and **6**[16] (90%). The reaction of these dienes with a catalytic amount of the Grubbs metallocarbene complex $RuCl_2(CHC_6H_5)[P(C_6H_{11})_3]_2$ yielded the dihydrofuran metathesis products **7** (78%) and **8**[16] (90%).[17,18]



Scheme 3. *Reagents and conditions*: (a) $(CH_3)_3S^+I^-$/BuLi/THF, −10°C to rt, 2–3.5 h. (b) i. NaH/THF, 0–65°C, 1 h. ii. Allyl bromide, rt, 1–2 h. (c) $(Cy_3P)_2Cl_2Ru{=}CHPh/CH_2Cl_2$, rt, 4 h.

Several epoxidation methods tested with dihydrofurans **7** and **8** resulted in recovering the starting material, low conversion or decomposition. Only *m*-CPBA epoxidation[17b] was successful (Scheme 4), and controlling the temperature and reaction time enabled the yield of the resulting epoxide to be optimised, although the selectivity remained the same (entries 1, 2 and 3, 4 in Table 1). Results were best at room temperature (entries 1 and 3), whereas at lower temperature the reaction was much slower (entries 2 and 4). The bulkier trityl group (entries 1 and 2) gave better selectivity than the less sterically demanding benzyl group (entries 3 and 4).[19] Epoxidations of **7** and **8** with *m*-CPBA in THF (vide infra) resulted in the recovery of the starting dihydrofurans.

We decided to continue with product **9** protected with the trityl group (Scheme 4), since it was obtained with better selectivity. The treatment of epoxide **9** with sodium azide under S_N2 conditions (Table 2, entry 1) gave epoxide opening products **13**/**14** in a high yield (80%), and 88:12 selectivity.[20,21] We also explored the opening of the minor epoxide **11**, which gave a slightly

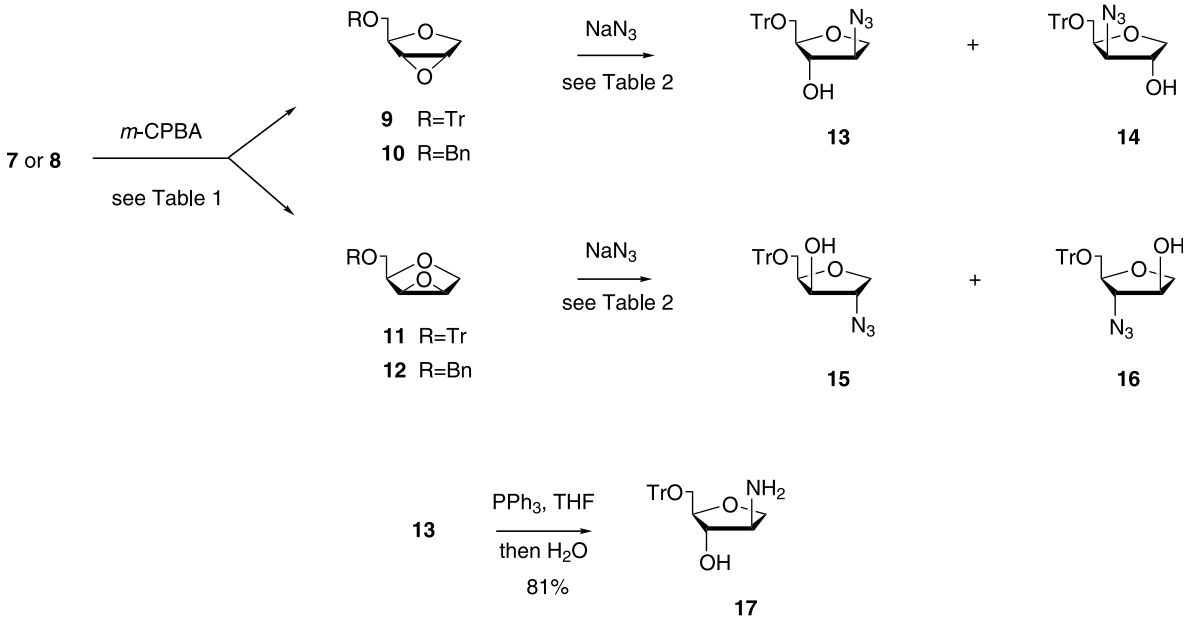


Scheme 2.

Table 1. Epoxydation of dihydrofurans **7** and **8**

Entry	Dihydrofuran	Conditions	Yield (%)[a]	Selectivity (*t*:*c*)[b]
1	**7**	*m*-CPBA, CH_2Cl_2, 25°C, 3 h	85	**9**/**11** (75:25)
2	**7**	*m*-CPBA, CH_2Cl_2, 0°C, 30 h	54	**9**/**11** (75:25)
3	**8**	*m*-CPBA, CH_2Cl_2, 25°C, 24 h	78	**10**/**12** (54:46)
4	**8**	*m*-CPBA, CH_2Cl_2, 0°C, 48 h	75	**10**/**12** (54:46)

[a] Isolated yield.
[b] Determined by integration in ^1H NMR.



Scheme 4.

Table 2. Opening of epoxides **9** and **11** with NaN_3

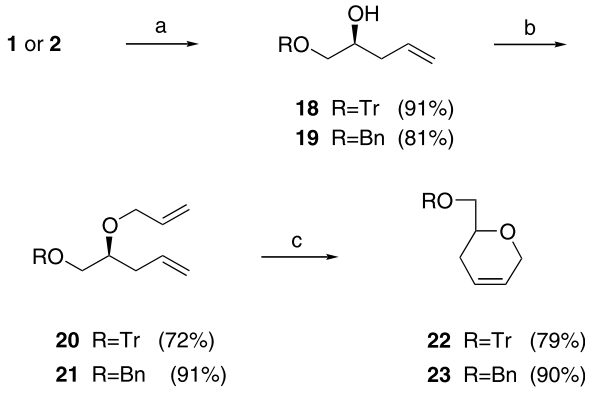
Entry	Epoxide	Conditions	Yield (%) [a]	Selectivity[b]
1	**9**	NaN_3, 15-crown-5, DMF, 80°C, 24 h	80	**13**:**14** = 88:12
2	**11**	NaN_3, 15-crown-5, DMF, 100°C, 24 h	72	**15**:**16** = 68:32
3	**11**	NaN_3, $LiClO_4$, CH_3CN, 85°C, 20 h	78	**15**:**16** = 83:17

[a] Isolated yield.
[b] Determined by integration in ^1H NMR.

lower yield and poorer selectivity (entry 2), as a consequence of the more similar stereoelectronic environment of both epoxide carbons. The presence of a lithium ion (entry 3), which chelates both the epoxide oxygen and the oxygen in the lateral chain,[22–26] allows the regioselective epoxide opening, thus favouring the formation of the *trans* azidoalcohol **15** (78% yield, with a 83:16 selectivity).

The major azidoalcohol product of the synthesis **13** was reduced under Staudinger conditions[27] in good yield (Scheme 4). This completed the synthesis of the desired 2-amino-1,4-anhydro-D-*arabino*-pentitol **17**.

The above synthesis can easily be extended to obtain aminohexitols. The formation of the 2*H*-dihydropyrans was completed following a similar route (Scheme 5). Opening glycidols **1** and **2** with allylmagnesium bromide–copper cyanide[28] afforded compounds **18**[29] and **19** in good yields. Allylation provided the dienes **20**,[29] and **21**, and the subsequent metathesis afforded the 2*H*-dihydropyrans **22**[30] and **23** in a 57 and 82% yield after the two steps, respectively.[17b]



Scheme 5. *Reagents and conditions*: (a) CuCN/allylmagnesium bromide/ether or THF, –78°C, 2 h. (b) i. NaH/THF, 0–65°C, 1 h. ii. Allyl bromide, rt, 2–4.5 h. (c) $(Cy_3P)_2Cl_2Ru{=}CHPh/CH_2Cl_2$, rt, 2.5–3 h.

We performed some epoxidations of 2*H*-dihydropyran **23**,[17b] but we obtained an inseparable mixture of the possible diastereomers. For this reason, we decided to continue the synthesis with trityl as the protecting

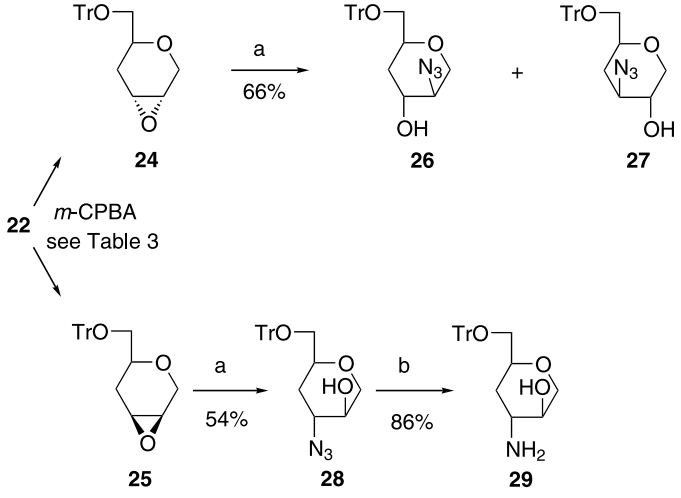
group **22**. In this case, the $TrOCH_2$ on the lateral chain is in the homoallylic position, and, therefore, its effect on the selectivity of epoxidation is expected to be lower. This was in fact the case at room temperature (Scheme 6; Table 3, entry 1), giving the mixture of epoxides **24**[31] and **25** in 68% yield (ratio 60:40) when **22** was treated with *m*-CPBA. The epoxidation at 4°C did not improve the selectivity, and made the reaction considerably slower (entry 2). The selectivity increased slightly when the solvent was heated to reflux, but the yield was considerably lower, probably due to partly deprotection of the trityl group in the acidic medium caused by the *m*-chlorobenzoic acid that was generated as a by-product of the reaction (entry 3).

The larger proportion of *cis*-epoxide in this case may be explained by the smaller steric hindrance of the trityloxymethyl chain and by the possible directing effect of the exocyclic oxygen through hydrogen bond formation with the *m*-CPBA. It has been reported that the addition of a solvent that competes in the formation of hydrogen bonds affects the diastereoselectivity.[32] In this case, the epoxidation in THF (Table 3, entry 4) slightly increased the selectivity towards the *trans* isomer **24**, with no loss in the yield (70%, ratio 67:33).

Table 3. Epoxidation of the 2*H*-dihydropyran **22**

Entry	Conditions	Yield (%) [a]	Selectivity (*t*:*c*)[b]
1	*m*-CPBA, CH_2Cl_2, 25°C, 24 h	68	**24**/**25** (60:40)
2	*m*-CPBA, CH_2Cl_2, 4°C, 43 h	53	**24**/**25** (40:40)
3	*m*-CPBA, CH_2Cl_2, 40°C, 43 h	26	**24**/**25** (64:36)
4	*m*-CPBA, THF, 25°C, 24 h	70	**24**/**25** (67:33)

[a] Isolated yield.
[b] Determined by integration in ^1H NMR.



Scheme 6. *Reagents and conditions*: (a) NaN_3, 15-crown-5, DMF, 100°C, 18–24 h. (b) PPh_3, THF, rt, 4 h; then H_2O, 65°C, 1 h.

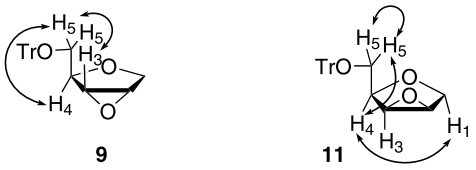


Figure 1. NOE enhancements in epoxides **9** and **11**.

Table 4. Comparison of δ in H3, H4 and C3, C4 of compounds **13**, **14**, **15** and **16**

	δ (H2)	δ (H3)	δ (C2)	δ (C3)
13	3.94	4.13	67.2	78.4
14	4.42	4.00	76.1	68.7
15	4.05	4.30	67.5	77.2
16	4.10	3.77	74.7	69.3

The reaction of the epoxide **24** with sodium azide in S_N2 conditions afforded the mixture of *trans* **26**/**27** azidoalcohols in 66% yield and 91:9 selectivity (Scheme 6), favouring the expected *trans* diaxial opening product **26**. Unfortunately, this mixture was chromatographically inseparable under the systems tested. On the other hand, under these conditions the epoxide **25** gave exclusively the *trans* diaxial azidoalcohol **28** in pure form in 54% yield. However, when the reaction was repeated with the addition of lithium perchlorate an inseparable mixture of diastereoisomers was also obtained. The isolated compound **28** was also reduced with triphenylphosphine–water to finally furnish the 3-amino-1,5-anhydro-3,4-dideoxy-*arabino*-alditol **29** in 86% yield.

2.1. Structural elucidation

In the following compounds, protons and carbons were assigned after selective proton irradiation to deduce connectivity, DEPT and heteronuclear correlation (HETCOR) experiments.

2.1.1. Epoxytetrahydrofurans 9 and 11 and azidopentitols 13, 14, 15 and 16. The configuration of epoxides **9** and **11** was deduced by studying NOE effects. In particular, the *trans* isomer **9** shows a NOE enhancement between H5 and H3, which is absent in **11** (Fig. 1).

The regio- and stereoisomers of anhydroazidopentitols were identified after the carbons and protons had been assigned (see Table 4), considering: (a) the S_N2 opening of epoxides **9** (to give **13** and **14**) and **11** (to furnish **15** and **16**); (b) both the proton and carbon bounded to the hydroxyl group appear at lower fields (δ_H >4 ppm, δ_C >74 ppm) than the CHN_3 unit ($\delta_H \leq 4$ ppm, $\delta_C \leq 70$ ppm). The relative configurations were confirmed by NOE experiments carried out in azidoalcohols **13** and **14**.

2.1.2. Epoxytetrahydropyrans 24 and 25 and azidohexitols 26 and 28. The relative configuration of epoxides **24** and **25** was elucidated by comparing the coupling con-

stants $^3J_{1eq,2}$ and $^3J_{3,4eq}$ with the values reported in the bibliography.[33] For both compounds $^3J_{4ax,5}$ (around 11 Hz) is consistent with the bulky CH_2OTr chain at C5 being in pseudo-equatorial position.

The assignation of the protons and carbons of azido-alcohols **26** and **28** also showed, as in the tetrahydrofuran series, that the proton and carbon of the azidomethyne unit appear at higher fields than those bounded to the hydroxyl group. The relative configuration was elucidated after a qualitative analysis of the coupling constants, which indicated that in both cases the azido-hydroxy groups are in pseudo-axial positions in a distorted chair conformation, and that the trityloxymethylene group adopts an equatorial disposition.

3. Conclusion

In summary, we have completed a stereoselective synthesis of 2-amino-1,4-anhydro-D-*arabino*-pentitol and 3-amino-1,5-anhydro-D-*arabino*-hexitol from commercially available (*R*)-glycidol, using a metathesis reaction for the key formation of the dihydrofuran and dihydro-2*H*-pyran. The method allows the synthesis of the L-enantiomers by simply changing the starting material to (*S*)-glycidol.

4. Experimental

4.1. General procedures

Melting points are uncorrected. Optical rotations were measured at 25°C in 10 cm cells. ^1H and ^{13}C NMR spectra were recorded at 300 or 400 MHz (300, 75.4 and 400, 100.5 MHz, respectively) Varian equipment, with $CDCl_3$ as solvent, unless otherwise specified. Coupling constants are given in hertz (Hz). Elemental analyses were determined at the Servei de Recursos Científics (Universitat Rovira i Virgili). Flash column chromatography was performed using silica gel 60 A CC (40–63 microns). Radial chromatography was performed on 1, 2 or 4 mm plates of silica gel, depending on the amount of product. Medium pressure chromatography (MPLC) was performed using silica gel 60 A CC (6–35 microns). Band separation was monitored by UV. TLC plates were prepared by using Kieselgel 60 PF_{254}. Solvents for chromatography were distilled at atmospheric pressure prior to use. Reaction solvents were purified and dried by using standard procedures.[34]

4.2. General procedure for the allylation reaction

Sodium hydride (60%, 3.0 mmol) was placed in an oven-dried flask and dispersed in anhydrous THF (4.0 mL). The corresponding alcohol (1.0 mmol), dissolved in dry THF (0.5 mL), was dropwise added to the reaction flask at 0°C. The mixture was slowly warmed to room temperature, and then heated to reflux for 1 h. The reaction mixture was cooled again to room temperature, and allyl bromide (3.0 mmol) was dropwise added. The reaction was controlled by TLC, and quenched by adding a few mL of ammonium chloride (aq., sat.) at 0°C. The contents of the flask were poured over water, and then extracted with ether. The combination of organic phases was dried over magnesium sulfate, filtered and the solvent evaporated under reduced pressure. The crude reaction mixture was purified by column chromatography to yield the pure diene.

4.3. General procedure for the metathesis reaction

The diene (1.00 mmol) was dissolved in anhydrous, degassed dichloromethane (40 mL) in a flame-dried, round-bottomed flask. Ethylene was bubbled in this solution for 5 min, and then the ruthenium catalyst $(Cy_3P)_2Cl_2Ru{=}CHPh$ (58 mg, 0.07 mmol), dissolved in 10 mL of dry and deoxygenated dichloromethane, was added to the solution. Ethylene was bubbled again for a further 5 min, and the mixture was stirred at room temperature under an argon atmosphere. The reaction was monitored by TLC, and after completion the solvent was evaporated at reduced pressure, and the reaction crude was filtered through Celite and finally purified by column chromatography to afford the corresponding heterocycle.

4.4. General procedure for the epoxidation reaction

The tetrahydropyran or tetrahydrofuran (1.00 mmol) was dissolved in dichloromethane (8.3 mL) and MCPBA (1.71 mmol) was added in one portion at the required temperature. The mixture was stirred, and finally quenched by pouring into $NaHCO_3$ (aq., sat.), and extracted with dichloromethane. The combination of organic phases was dried over magnesium sulfate and filtered, and the solvent was then evaporated under reduced pressure. Purification by column chromatography yielded the pure epoxide.

4.5. General procedure for the epoxide opening with sodium azide

To a solution of the epoxide (1 mmol) in anhydrous DMF (4.3 mL), sodium azide (80 mg, 1.23 mmol) and the crown ether 15-crown-5 (0.64 mmol) were sequentially added, and the mixture was heated to the desired temperature. Once the reaction had finished, the crude was filtered through silica gel, eluting with dichloromethane. The organic solvent was evaporated under reduced pressure, and the product was purified by column chromatography.

4.6. General procedure for the epoxide opening with sodium azide with the addition of lithium perchlorate

In a perfectly dry round-bottomed flask, the corresponding epoxide (1 mmol) was dissolved in a 2.0 M solution of lithium perchlorate in acetonitrile (5 mL). Then, sodium azide (325 mg, 5.00 mmol) was added, and the mixture was heated to 85°C under an argon atmosphere for 24 h. The reaction mixture was subsequently cooled to room temperature, and then filtered through silica gel, using dichloromethane as eluent. The

organic solvent was then evaporated, and the crude was purified by column chromatography to furnish the desired hydroxyazide.

4.7. General procedure for the azide reduction

Triphenylphosphine (393 mg, 1.5 mmol) was added to a solution of the azide (1 mmol) in anhydrous THF (4.6 ml) and the reaction mixture was stirred until TLC control showed that the starting material had been completely consumed. At this point, water (360 μL, 20 mmol) was added and the mixture was stirred for 1 h at reflux. The solvent was then evaporated at reduced pressure, and the amine was finally purified by column chromatography (eluting with CH_2Cl_2 and then with CH_2Cl_2/MeOH 30:1).

4.8. (*S*)-1-*O*-Trityl-but-3-en-1,2-diol 3

In a two-necked flask, the salt $(CH_3)_3S^+I^-$ (4.84 g, 23.7 mmol) was dissolved in THF (73.0 mL), and then BuLi (2.5 M in hexanes, 9.2 mL, 23.0 mmol) was added at −10°C. The mixture was stirred for 30 min, and then the epoxide **1** (2.50 g, 7.90 mmol), dissolved in THF (7.3 mL), was added dropwise. The reaction was slowly warmed to rt. After 2 h, dimethyl sulfide was removed with an argon stream, the flask was cooled to 0°C, and water was added dropwise. The mixture was extracted with ethyl ether, and the combination of organic phases was dried over magnesium sulfate and filtered. The crude obtained after evaporation of the solvent was purified by column chromatography (ethyl ether/petroleum ether 40–60°, gradually increasing the polarity from 1:2 to 1:1) to afford pure **3** as a syrup (1.80 g, 69%). $[\alpha]_D^{25} = -2.5$ (*c* 1.1, CH_2Cl_2). IR (neat): *v* 3430, 1596, 1490, 1445, 1075, 768, 740 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.21 (m, 15H), 5.80 (ddd, 1H, *J* 17.4, 10.6, 5.7), 5.30 (dt, 1H, *J* 17.4, 1.8), 5.15 (ddd, 1H, *J* 10.6, 1.8, 1.5), 4.27 (m, 1H), 3.21 (dd, 1H, *J* 9.3, 3.9), 3.11 (dd, 1H, *J* 9.3, 7.4), 2.46 (bs, 1H). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ in ppm: 143.7, 136.9, 128.6, 127.8, 127.1, 116.3, 86.7, 71.9, 67.4. Anal. calcd for $C_{23}H_{22}O_2$: C, 83.60; H, 6.71. Found: C, 83.91; H, 6.51.

4.9. (*S*)-2-*O*-Allyl-1-trityl-but-3-en-1,2-diol

The method for the synthesis of **3** was followed, starting from **2** (864 mg, 5.26 mmol), $(CH_3)_3S^+I^-$ (3.22 g, 15.78 mmol), BuLi (6.1 mL, 12.25 mmol) in THF (56.5 mL). The reaction was completed after 3 h 30 min. After the treatment previously described, column chromatography (ethyl ether/petroleum ether 40–60°, gradually increasing the polarity from 1:4 to 1:1) furnished alkenol **4** (769 mg, 82%) as a syrup. $[\alpha]_D^{25} = -0.4$ (*c* 1.0, CH_2Cl_2). IR (neat): *v* 3435, 1596, 1496, 1443, 1098, 768, 699 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 5.83 (ddd, 1H, *J* 17.5, 10.7, 5.6), 5.35 (dt, 1H, *J* 17.5, 1.5), 5.19 (dt, 1H, *J* 10.7, 1.5), 4.56 (m, 2H), 4.34 (m, 1H), 3.53 (dd, 1H, *J* 9.6, 3.3), 3.37 (dd, 1H, *J* 9.3, 7.6), 2.63 (bs, 1H). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ in ppm: 137.7, 136.5, 128.4, 127.8, 127.7, 116.4, 73.9, 73.3, 71.4. Anal. calcd for $C_{22}H_{20}O_2$: C, 74.13; H, 7.92. Found: C, 73.94; H, 8.28.

4.10. (*S*)-2-*O*-Allyl-1-benzyl-but-3-en-1,2-diol 5

The general method for the allylation reaction was applied, starting from **3** (1.80 g, 5.45 mmol), NaH (60%, 654 mg, 16.4 mmol), allyl bromide (1.40 mL, 16.4 mmol) in anhydrous THF (25 mL). The reaction was quenched after 2 h, and the crude was purified by column chromatography (ethyl ether/petroleum ether 40–60° 1:4) to yield **5** (1.73 g, 92%) as a colourless syrup. $[\alpha]_D^{25} = -6.6$ (*c* 1.2, CH_2Cl_2). IR (neat): *v* 1597, 1490, 1447, 1077, 767, 704 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.10 (m, 15H), 5.93 (m, 1H), 5.74 (ddd, 1H, *J* 17.4, 9.9, 7.2), 5.31 (ddd, 1H, *J* 18.9, 3.3, 1.8), 5.27 (ddd, 1H, *J* 17.4, 1.8, 1.2), 5.22 (ddd, 1H, *J* 9.9, 1.8, 1.2), 5.17 (ddd, 1H, *J* 10.5, 3.3, 1.2), 4.12 (ddd, 1H, *J* 13.0, 5.0, 1.2), 3.98 (ddd, 1H, *J* 13.0, 5.7, 1.2), 3.94 (m, 1H), 3.27 (dd, 1H, *J* 9.6, 6.4, 1.2), 3.07 (dd, 1H, *J* 9.6, 5.1). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ in ppm: 144.0, 136.3, 135.0, 128.7, 127.7, 126.9, 117.7, 116.5, 86.5, 79.6, 69.8, 66.6. Anal. calcd for $C_{26}H_{26}O_2$: C, 84.29; H, 7.07. Found: C, 84.34; H, 7.02.

4.11. (*S*)-2-*O*-Ally1-*O*-benzyl-but-3-en-1,2-diol 6

The general method for the allylation reaction was applied, starting from **4** (874 mg, 4.90 mmol), NaH (60%, 589 mg, 14.7 mmol), allyl bromide (1.30 mL, 15.2 mmol) in anhydrous THF (22 mL). The reaction was quenched after 1 h, and the crude was purified by column chromatography (ethyl ether/petroleum ether 40–60° 1:5) to give compound **6** (778 mg, 82%) as a colourless syrup. $[\alpha]_D^{25} = +1.1$ (*c* 1.3, CH_2Cl_2). IR (neat): *v* 1644, 1453, 1205, 738, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.25–7.08 (m, 5H), 5.92 (dddd, 1H, *J* 17.3, 10.3, 6.0, 5.2), 5.76 (ddd, 1H, *J* 17.5, 10.4, 6.6), 5.30 (ddd, 1H, *J* 17.5, 1.8, 1.2), 5.29 (ddd, 1H, *J* 17.3, 3.2, 1.6), 5.26 (ddd, 1H, *J* 10.4, 1.8, 0.8), 5.17 (ddd, 1H, *J* 10.3, 3.2, 1.4), 4.61 (d, 1H, *J* 12.0), 4.56 (d, 1H, *J* 12.0), 4.27 (ddd, 1H, *J* 13.4, 5.2, 1.6), 4.00 (m, 1H), 3.94 (dtd, 1H, *J* 13.4, 6.0, 1.6), 3.55 (dd, 1H, *J* 10.2, 6.4, 1.6), 3.50 (dd, 1H, *J* 10.2, 4.4). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ in ppm: 138.2, 135.7, 134.8, 128.3, 127.6, 127.5, 118.2, 116.8, 79.3, 73.3, 72.8, 69.6. Anal. calcd for $C_{22}H_{20}O_2$: C, 77.03; H, 8.31. Found: C, 77.08; H, 8.67.

4.12. (*S*)-2-Trityloxymethyl-2,5-dihydrofuran 7

Starting from diene **5** (1.85 g, 5.40 mmol), ruthenium catalyst (291 mg, 0.35 mmol) and dichloromethane (a total of 250 mL), the general procedure for the metathesis reaction was applied. The reaction was completed in 4 h, and after purification (hexanes/ethyl acetate 10:1), compound **7** was isolated in pure form as a white solid (1.33 g, 78%). Mp = 102–109°C. $[\alpha]_D^{25} = -7.8$ (*c* 0.9, CH_2Cl_2). IR (neat): *v* 1596, 1490–1446, 1092, 761–702 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.48–7.18 (m, 15H), 5.96 (ddd, 1H, *J* 6.0, 4.0, 1.5), 5.80 (m, 1H), 5.00 (m, 2H), 4.71 (m, 2H), 3.15 (dd, 1H, *J* 9.3, 5.6), 3.10 (dd, 1H, *J* 9.3, 4.5). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ: 144.0, 128.7, 127.7, 127. 6, 127.4, 126.9, 86.3, 85.4, 75.5, 66.5. Anal. calcd for $C_{24}H_{22}O_2$: C, 84.18; H, 6.48. Found: C, 83.95; H, 6.17.

4.13. (*S*)-2-Benzyloxymethyl-2,5-dihydrofuran 8

Starting from diene **6** (571 mg, 2.62 mmol), ruthenium catalyst (153 mg, 0.19 mmol) and dichloromethane (a total of 130 mL), the general procedure for the metathesis reaction was applied. The reaction was completed in 4 h, and after purification (hexanes/ethyl acetate 7:1), the clear syrup **8** was isolated in pure form (447 mg, 90%). $[\alpha]_D^{25} = -98.1$ (*c* 1.4, CH_2Cl_2). IR (neat): *v* 1720, 1502–1458, 1087, 721–690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.09 (m, 5H), 5.96 (dd, 1H, *J* 6.0, 1.6), 5.80 (m, 1H, *J* 10.0), 4.99 (m, 2H), 4.65 (m, 2H), 4.61 (d, 1H, *J* 12.4), 4.56 (d, 1H, *J* 12.4), 3.51 (d, 2H, *J* 5.2). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 138.1, 128.2, 128.0, 127.5, 127.4, 126.8, 85.3, 75.3, 73.2, 72.6. Anal. calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 76.00; H, 7.27.

4.14. (2*R*,3*S*,4*S*)-3,4-Epoxy-2-trityloxymethyl-tetrahydrofuran 9 and (2*S*,3*R*,4*R*)-3,4-epoxy-2-trityloxymethyl-tetrahydrofuran 11

Starting from the dihydrofuran **7** (108 mg, 0.32 mmol), MCPBA (133 mg, 0.54 mmol) and anhydrous CH_2Cl_2 (2.6 mL), the general procedure for the epoxidation reaction was applied. The reaction was stirred for 3 h at room temperature. After the conventional work-up, column chromatography (gradually increasing the polarity from hexanes:ethyl acetate, 10:1 to 5:1) allowed the isolation of **9** (72 mg, 64%) and **11** (24 mg, 21%), both as transparent needles.

9: mp = 155–157°C. $[\alpha]_D^{25} = +4.83$ (*c* 0.8, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.48–7.18 (m, 15H), 4.21 (t, 1H, *J* 4.2), 4.08 (d, 1H, *J* 10.2), 4.01 (d, 1H, *J* 10.2), 3.90 (d, 1H, *J* 3.0), 3.72 (d, 1H, *J* 3.0), 3.31 (dd, 1H, *J* 10.2, 4.8), 3.16 (dd, 1H, *J* 10.2, 3.7). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 144.1, 128.6, 127.9, 127.1, 86.8, 77.0, 68.0, 64.1, 58.1, 56.6. Anal. calcd for $C_{24}H_{22}O_3$: C, 80.42; H, 6.19. Found: C, 80.34; H, 6.58.

11: mp = 118–120°C. $[\alpha]_D^{25} = -20.4$ (*c* 1.4, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.53–7.26 (m, 15H), 4.06 (d, 1H, *J* 10.4), 4.03 (m, 1H), 3.94 (d, 1H, *J* 2.6), 3.82 (d, 1H, *J* 2.6), 3.75 (d, 1H, *J* 10.8), 3.41 (dd, 1H, *J* 9.0, 5.4), 3.34 (dd, 1H, *J* 9.0, 7.4). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 143.6, 128.5, 127.8, 127.6, 86.8, 76.5, 67.6, 62.2, 56.9, 56.2. Anal. calcd for $C_{24}H_{22}O_3$: C, 80.42; H, 6.19. Found: C, 80.17; H, 6.26.

4.15. (2*R*,3*S*,4*S*)-2-Benzyloxymethyl-3,4-epoxy-tetrahydrofuran 10 and (2*S*,3*R*,4*R*)-2-benzyloxymethyl-3,4-epoxy-tetrahydrofuran 12

Starting from the dihydrofuran **8** (78 mg, 0.41 mmol), MCPBA (173 mg, 0.70 mmol) and anhydrous CH_2Cl_2 (3.4 mL), the general procedure for the epoxidation reaction was applied. The reaction was stirred for 24 h at room temperature. After the conventional work-up, column chromatography (hexanes:ethyl acetate, 4:1) gave the mixture of diastereomers **10**/**12** as a yellowish syrup (66 mg, 78% yield, ratio 54:46). ^1H NMR (400 MHz, $CDCl_3$) δ (data of the mixture) 7.35–7.20 (m, 10H), 4.57 (d, 1H, *J* 11.8), 4.54 (s, 2H), 4.06 (d, 1H, *J* 10.4), 4.23 (t, 1H, *J* 4.4), 4.01 (d, 1H, *J* 10.0), 4.00 (t, 1H, *J* 6.2), 3.87 (d, 1H, *J* 10.0), 3.83–3.76 (m, 4H), 3.72 (d, 2H, *J* 10.4), 3.66 (d, 2H, *J* 6.4), 3.57 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ (data of the mixture) 138.7, 138.6, 130.1, 129.8, 128.4, 128.4, 128.2, 127.8, 127.7, 127.4, 76.7, 76.6, 73.6, 73.5, 70.2, 68.5, 67.7, 67.6, 57.8, 56.4, 56.6, 56.0.

4.16. 1,4-Anhydro-2-azido-2-deoxy-5-*O*-trityl-D-*arabino*-pentitol 13 and 1,4-anhydro-3-azido-3-deoxy-5-*O*-trityl-D-*xylo*-pentitol 14

Starting from the epoxide **9** (160 mg, 0.45 mmol), sodium azide (44 mg, 0.67 mmol), 15-crown-5 (56 μL, 0.28 mmol) and anhydrous DMF (2 mL), the general procedure for the epoxide opening reaction was applied. The reaction was stirred for 24 h at 100°C. After purification by column chromatography (hexanes:ethyl acetate, 5:1) the azides **13** (126 mg, 70% yield) and **14** (18 mg, 10% yield) were isolated as clear syrups.

13: $[\alpha]_D^{25} = -2.3$ (*c* 0.7, CH_2Cl_2). IR (neat): *v* 3050, 1448, 1595, 1264, 810–705 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.20 (m, 15H), 4.13 (dd, 1H, *J* 5.2, 4.0), 4.06 (dd, 1H, *J* 9.4, 6.0), 3.94 (dt, 1H, *J* 6.0, 4.0), 3.83 (dd, 1H, *J* 9.4, 4.0), 3.82 (m, 1H), 3.36 (dd, 1H, *J* 9.6, 6.0), 3.22 (dd, 1H, *J* 9.6, 5.2). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.4, 128.4, 127.8, 127.0, 86.5, 83.7, 78.4, 70.2, 67.2, 63.8. Anal. calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 71.58; H, 5.88; N, 10.89.

14: $[\alpha]_D^{25} = -5.8$ (*c* 0.3, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45–7.20 (m, 15H), 4.42 (m, 1H), 4.32 (ddd, 1H, *J* 6.8, 6.0, 4.0), 4.08 (dd, 1H, *J* 10.2, 4.4), 4.00 (dd, 1H, *J* 4.0, 2.0), 3.70 (dd, 1H, *J* 10.2, 2.0), 3.45 (dd, 1H, *J* 9.6, 5.8), 3.19 (dd, 1H, *J* 9.6, 6.8). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.6, 128.5, 127.7, 126.9, 86.3, 78.6, 76.1, 73.8, 68.7, 62.1. Anal. calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 71.89; H, 6.00; N, 10.04.

4.17. 1,4-Anhydro-2-azido-2-deoxy-5-*O*-trityl-D-*xylo*-pentitol 15 and 1,4-anhydro-3-azido-3-deoxy-5-*O*-trityl-D-*arabino*-pentitol 16

Starting from the epoxide **11** (50 mg, 0.14 mmol), sodium azide (45 mg, 0.70 mmol), lithium perchlorate (148 mg, 1.39 mmol) and anhydrous acetonitrile (0.7 mL), the general procedure for the epoxide opening reaction with lithium perchlorate was applied. The reaction was stirred for 20 h at 85°C. After purification by column chromatography (hexanes:ethyl acetate, 5:1) the azides **15** (36 mg, 64% yield) and **16** (8 mg, 14% yield) were isolated, as colourless syrups.

15: $[\alpha]_D^{25} = +32.6$ (*c* 1.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.21 (m, 15H), 4.30 (m, 1H), 4.27 (dd, 1H, *J* 10.0, 4.8), 4.12 (m, 1H), 4.05 (m, 1H), 3.82 (dd, 1H, *J* 10.0, 2.0), 3.50 (dd, 1H, *J* 10.0, 5.2), 3.37 (dd, 1H, *J* 10.0, 3.9). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.0, 128.2, 128.0, 127.2, 86.4, 78.8, 77.2, 70.4, 67.5, 62.4.

Anal. calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 71.56; H, 6.12; N, 9.92.

16: $[\alpha]_D^{25} = +21.8$ (*c* 0.8, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.15 (m, 15H), 4.10 (m, 1H), 3.91 (d, 1H, *J* 9.6), 3.81 (dd, 1H, *J* 9.6, 3.6), 3.79 (m, 1H), 3.77 (m, 1H), 3.52 (dd, 1H, *J* 10.4, 3.6), 3.12 (dd, 1H, *J* 9.6, 2.8). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.1, 128.9, 128.2, 128.1, 86.2, 82.8, 77.3, 74.7, 69.3, 64.3. Anal. calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 71.64; H, 5.68; N, 10.07.

4.18. 2-Amino-1,4-anhydro-2-deoxy-5-*O*-trityl-D-*arabino*-pentitol 17

Starting from the azidoalcohol **13** (245 mg, 0.61 mmol), triphenylphosphine (240 mg, 0.92 mmol), anhydrous THF (3.0 mL) and water (170 μL, 12.1 mmol) the general procedure for the azide reduction was applied. Once the reaction was complete (4 h), column chromatography (CH_2Cl_2/methanol from 50:1 to 20:1) afforded the aminoalcohol **17** (185 mg, 81%) in pure form as a clear syrup. $[\alpha]_D^{25} = +11.5$ (*c* 1.2, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.17 (m, 15H), 4.01 (dd, 1H, *J* 8.8, 5.6), 3.83 (m, 2H), 3.60 (dd, 1H, *J* 8.8, 4.4), 3.33 (dd, 1H, *J* 8.0, 4.8), 3.28 (m, 2H), 2.50 (bs, 3H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.5, 128.6, 127.7, 127.0, 86.9, 83.9, 80.1, 73.8, 64.4, 59.7. Anal. calcd for $C_{24}H_{25}NO_3$: C, 76.77; H, 6.71; N, 3.73. Found: C, 76.55; H, 6.54; N, 3.45.

4.19. (*S*)-1-*O*-Benzyl-pent-4-en-1,2-diol 19

CuCN (2.48 g, 30.0 mmol) was placed in a flask under argon and dried by gently heating with a flame under vacuum. It was then allowed to cool under a positive pressure of argon. This process was repeated three times and then ether (43 ml) was added. The resulting mixture was stirred to form a slurry, cooled to −78°C and then vinylmagnesium chloride (58.5 mL, 60.0 mmol) was added dropwise over a period of 15 min. The heterogeneous mixture was warmed to −20°C until the CuCN completely dissolved and it was then cooled again to −78°C. A solution of **2** (2.14 g, 13.0 mmol) in 43 mL of dry ether was added dropwise. The resulting mixture was warmed to −60°C and stirred for 2 h. The reaction was monitored by TLC in EtOAc/Hex = 1:10, quenched by adding an aqueous solution (10% concentrated NH_4OH–90% saturated NH_4Cl) and warmed to ambient temperature with vigorous stirring until the solids dissolved. The mixture was extracted with ether, and the combination of extracts was washed with water and then with brine. The ethereal solution was dried, filtered and concentrated to dryness. Column chromatography purification (EtOAc/Hex = 1:10) afforded alcohol **19** (2.26 g, 90%) as a syrup. $[\alpha]_D^{25} = +2.8$ (*c* 1.2, CH_2Cl_2). IR (neat): *v* 3427, 1641, 1453, 1207, 739, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46–7.42 (m, 5H), 5.82 (ddt, 1H, *J* 18.6, 8.6, 5.0), 5.10 (m, 2H), 4.58 (s, 2H), 3.91 (m, 1H), 3.50 (ddd, 1H, *J* 9.6, 3.6, 0.8), 3.39 (m, 1H), 2.53 (bs, 1H), 2.26 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ: 137.8, 134.2, 128.4, 127.7, 127.6, 117.6, 73.8, 73.3, 69.6, 37.8. Anal. calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.62; H, 8.71.

4.20. (*S*)-2-*O*-Allyl-1-*O*-benzyl-pent-4-en-1,2-diol 21

The general method for the allylation reaction was applied, starting from **19** (1.00 g, 5.20 mmol), NaH (60%, 624 mg, 15.6 mmol), allyl bromide (1.35 mL, 15.8 mmol) in anhydrous THF (23.6 mL). The reaction was quenched after 4 h 30 min, and the crude was purified by column chromatography (hexane/ethyl acetate, 15:1) to afford the colourless syrup **21** (1.10 g, 91%). $[\alpha]_D^{25} = -1.4$ (*c* 1.3, CH_2Cl_2). IR (neat): *v* 1642, 1453, 1116, 738, 686 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.21–7.03 (m, 5H), 5.96 (m, 1H), 5.81 (ddt, 1H, *J* 14.7, 7.6, 5.1), 5.28 (ddd, 1H, *J* 17.4, 3.3, 1.5), 5.15 (ddd, 1H, *J* 9.9, 3.3, 1.5), 5.09 (ddd, 1H, *J* 14.7, 3.6, 1.2), 5.04 (ddd, 1H, *J* 7.6, 3.6, 1.2), 4.38 (s, 2H), 4.13 (ddt, 1H *J* 12.6, 5.6, 1.7), 4.06 (ddt, 1H, *J* 12.6, 5.4, 1.5), 3.59 (m, 1H), 3.51 (d, 2H, *J* 4.8), 3.33 (m, 2H). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ: 138.3, 135.2, 134.5, 128.3, 127.6, 127.5, 117.1, 116.6, 77.5, 73.3, 72.0, 70.8, 36.2. Anal. calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.24; H, 8.80.

4.21. (*S*)-2-Trityloxymethyl-3,6-dihydro-2*H*-pyran 22

Starting from diene **20** (400 mg, 1.04 mmol), ruthenium catalyst (61 mg, 0.08 mmol) and dichloromethane (a total of 63 mL), the general procedure for the metathesis reaction was applied. The reaction was completed in 3 h, and after purification (hexanes/ethyl acetate, 50:1), compound **22** was isolated in pure form as a white solid (294 mg, 79%). Mp = 118–120°C. $[\alpha]_D^{25} = -67.5$ (*c* 1.1, CH_2Cl_2). IR (neat): *v* 1596, 1489–1445, 1090, 767–703 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45–7.24 (m, 15H), 5.81 (ddd, 1H, *J* 10.0, 5.2, 2.0), 5.74 (m, 1H), 4.22 (m, 2H), 3.78 (m, 1H), 3.26 (ddd, 1H, *J* 9.6, 6.0, 1.2), 3.03 (ddd, 1H, *J* 9.6, 5.6, 0.8), 2.05 (m, 2H). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 144.0, 128.7, 127.8, 126.9, 126.3, 123.9, 86.4, 73.0, 66.7, 65.9, 28.1. Anal. calcd for $C_{25}H_{24}O_2$: C, 84.24; H, 6.79. Found: C, 83.91; H, 7.18.

4.22. (*S*)-2-Benzyloxymethyl-3,6-dihydro-2*H*-pyran 23

Starting from diene **21** (535 mg, 2.30 mmol), ruthenium catalyst (135 mg, 0.17 mmol) and dichloromethane (a total of 115 mL), the general procedure for the metathesis reaction was applied. The reaction was completed in 2.5 h, and after purification (hexanes/ethyl acetate, 10:1), compound **23** was isolated as a syrup (423 mg, 90%). $[\alpha]_D^{25} = -8.0$ (*c* 1.2, CH_2Cl_2). IR (neat): *v* 1720, 1496–1452, 1091, 737–698 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H), 5.81 (m, 1H), 5.72 (dddd, 1H, *J* 18.8, 5.1, 2.6, 0.8), 4.64 (d, 1H, *J* 12.3), 4.56 (d, 1H, *J* 12.3), 4.23 (m, 2H), 3.79 (ddd, 1H, *J* 14.1, 6.3, 4.1), 3.52 (dd, 1H, *J* 10.5, 6.3), 3.47 (dd, 1H, *J* 10.5, 4.1), 2.09 (m, 1H), 1.92 (m, 1H). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 138.1, 128.3, 127.7, 127.6, 126.3, 123.6, 73.4, 72.9, 65.7, 72.6, 27.2. Anal. calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.74; H, 8.03.

4.23. (2*S*,4*R*,5*S*)-4,5-Epoxy-2-trityloxymethyl-tetrahydropyran 24 and (2*S*,4*R*,5*R*)-4,5-epoxy-2-trityloxymethyl-tetrahydropyran 25

Starting from the dihydropyran **22** (472 mg, 1.32 mmol), MCPBA (558 mg, 2.26 mmol) and anhydrous THF instead of CH_2Cl_2 (11 mL), the general procedure for the epoxidation reaction was applied. The reaction was stirred for 24 h at room temperature. After the conventional work-up, column chromatography (hexanes:ethyl acetate, 20:1) allowed the isolation of the mixture of **24** and **25** (345 mg, 70% yield, ratio 67:33). The diastereomeric mixture was separated by MPLC (gradually increasing the polarity from hexanes to hexanes: ethyl acetate 15:1), to furnish pure **24** (230 mg, 47%) and pure **25** (115 mg, 23%), as colourless syrups.

24: $[\alpha]_D^{25} = -26.8$ (*c* 1.1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.18 (m, 15H), 4.23 (dd, 1H, *J* 13.6, 4.0), 3.94 (d, 1H, *J* 13.6), 3.61 (m, 1H), 3.50 (m, 1H), 3.23 (t, 1H, *J* 4.0), 3.11 (dd, 1H, J 9.7, 6.2), 2.97 (dd, 1H, *J* 9.7, 4.8), 2.04 (dt, 1H, *J* 14.6, 2.4), 1.77 (ddd, 1H, *J* 14.6, 11.2, 1.8). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 143.8, 128.6, 127.7, 126.9, 86.3, 69.5, 66.3, 65.7, 51.2, 50.7, 28.2. Anal. calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.35; H, 6.53.

25: $[\alpha]_D^{25} = -33.5$ (*c* 1.1, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.10 (m, 15H), 4.13 (d, 1H, *J* 13.2), 3.74 (d, 1H, *J* 13.2), 3.32 (m, 1H), 3.25 (dd, 1H, *J* 5.6, 4.0), 3.13 (dd, 1H, *J* 9.5, 6.2), 2.96 (d, 1H, *J* 4.0), 2.82 (dd, 1H, *J* 9.5, 5.4), 1.87 (ddd, 1H, *J* 15.5, 5.6, 4.0), 1.67 (dd, 1H, *J* 15.5, 11.6). ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 143.8, 128.6, 127.7, 126.9, 86.4, 72.2, 66.2, 64.6, 49.5, 49.1, 26.8. Anal. calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.50; H, 6.70.

4.24. 1,5-Anhydro-2-azido-2,4-dideoxy-5-*O*-trityl-D-*arabino*-hexitol 26 and 1,5-anhydro-3-azido-3,4-dideoxy-5-*O*-trityl-D-*xylo*-hexitol 27

Starting from the epoxide **34** (126 mg, 0.34 mmol), sodium azide (26 mg, 0.41 mmol), 15-crown-5 (40 μL, 0.22 mmol) and anhydrous DMF (1.5 mL), the general procedure for the epoxide opening reaction was applied. The reaction was stirred for 24 h at 100°C. After purification by column chromatography (hexanes:ethyl acetate, 1:1) the unseparable mixture of diastereomeric azides **26**/**27** (93 mg, 66% yield, ratio 91:9) was isolated as a yellowish syrup.

26 (data from the mixture): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.18 (m, 15H), 4.00 (dd, 1H, *J* 12.4, 2.4), 3.94 (m, 1H), 3.93 (m, 1H), 3.84 (dd, 1H, *J* 12.4, 2.4), 3.25 (m, 1H), 3.20 (dd, 1H, *J* 9.6, 6.0), 3.01 (dd, 1H, *J* 9.6, 5.2), 1.86 (ddd, 1H, *J* 14.0, 10.8, 3.2), 1.63 (dt, 1H, *J* 14.0, 2.8). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.7, 128.5, 127.6, 126.8, 86.4, 71.2, 66.1, 66.0, 64.3, 59.6, 32.0.

27 (data from the mixture): ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.5, 128.4, 127.6, 126.8, 86.5, 75.4, 70.1, 65.8, 64.1, 60.5, 33.0.

4.25. 1,5-Anhydro-3-azido-3,4-dideoxy-5-*O*-trityl-D-*arabino*-hexitol 28

Starting from the epoxide **25** (105 mg, 0.28 mmol), sodium azide (22 mg, 0.34 mmol), 15-crown-5 (33 μL, 0.17 mmol) and anhydrous DMF (1.2 mL), the general procedure for the epoxide opening reaction was applied. The reaction was stirred for 18 h at 100°C. After purification by column chromatography (hexanes:ethyl acetate, 1:1) the azide **28** (63 mg, 54% yield) was isolated as a colourless syrup. $[\alpha]_D^{25} = -31.8$ (*c* 1.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.18 (m, 15H), 3.81 (dd, 1H, *J* 12.4, 1.2), 3.80 (m, 1H), 3.76 (m, 1H), 3.71 (dd, 1H, *J* 12.4, 2.0), 3.50 (m, 1H), 3.18 (dd, 1H, *J* 9.6, 5.6), 3.03 (dd, 1H, *J* 9.6, 4.8), 1.95 (dtd, 1H, *J* 14.8, 10.8, 3.6), 1.67 (dt, 1H, *J* 14.4, 3.2). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.5, 128.4, 127.6, 126.8, 86.5, 71.7, 67.5, 66.0, 66.2, 58.6, 27.9. Anal. calcd for $C_{25}H_{25}N_3O_3$: C, 72.27; H, 6.06; N, 10.11. Found: C, 72.38; H, 6.12; N, 10.49.

4.26. 1,5-Anhydro-3-amino-3,4-dideoxy-5-*O*-trityl-D-*arabino*-hexitol 29

Starting from the azidoalcohol **28** (85 mg, 0.20 mmol), triphenylphosphine (64 mg, 0.24 mmol), anhydrous THF (0.95 mL) and water (60 μL, 3.33 mmol) the general procedure for the azide reduction was applied. Once the reaction was completed (4 h), column chromatography (CH_2Cl_2/methanol from 50:1 to 30:1) afforded the aminoalcohol **29** (65 mg, 86%) in pure form as a clear syrup. $[\alpha]_D^{25} = -5.3$ (*c* 2.4, CH_3Cl). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.21 (m, 15H), 3.93 (dd, 1H, *J* 12.0, 2.0), 3.94 (m, 1H), 3.61 (dd, 1H, *J* 12.0, 4.0), 3.34 (m, 1H), 3.24 (dd, 1H, *J* 9.6, 6.0), 3.06 (q, 1H, *J* 4.2), 3.02 (dd, 1H, *J* 9.6, 5.2), 1.91 (ddd, 1H, *J* 14.0, 9.6, 4.2), 1.74 (bs, 3H), 1.47 (dt, 1H, *J* 14.0, 3.6). ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 143.6, 128.4, 127.7, 126.7, 86.3, 71.4, 70.3, 66.5, 65.2, 49.2, 32.3. Anal. calcd for $C_{25}H_{27}NO_3$: C, 77.09; H, 6.99; N, 3.60. Found: C, 77.22; H, 7.02; N, 3.98.

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