Synthesis of All Diastereomers of the 2-Deoxypentoses and the 2,6-Dideoxyhexoses from 2-Phenyl-1,3-dioxan-5-one Hydrate

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All diastereomers of the 2-deoxypentoses and the 2,6-dideoxyhexoses were synthesized from 2-phenyl-1,3-dioxan-5-one hydrate (**1**), by alkylation *via* the RAMP-hydrazone (**2**). Some of the diastereomers were synthesized in the racemic form via the dimethylhydrazone (**28**). The 2-deoxypentoses were synthesized by alkylation with allyl bromide, followed by stereoselective reduction, ozonolysis, and deprotection. The 2,6-dideoxypentoses were synthesized by dialkylation with allyl bromide and methyl iodide.

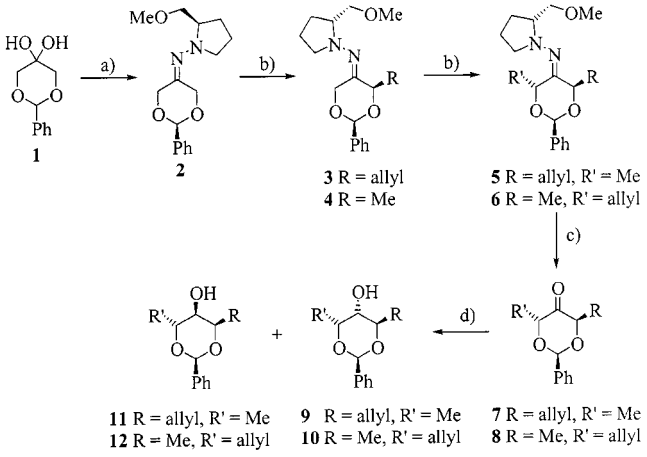
Introduction

Deoxysugars and deoxysugar oligosaccharides play a very important role in biology.[1] Because of the high density of stereogenic centers in these compounds, their synthesis from nonchiral compounds represent challenging synthetic problems. We have been interested in exploring the synthetic utility of the benzylidene-protected dihydroxyacetone (BDHA) and its hydrate, **1**. Recently we reported the synthesis of racemic 2-deoxyribose and 2-deoxyxylose from the readily available 2-phenyl-1,3-dioxan-5-one hydrate (**1**).[2] By taking advantage of Enders' auxiliaries SAMP or RAMP [(*S*)- or (*R*)-1-amino-2-(methoxymethyl)-pyrrolidine],[3] the enantioselective synthesis of 2-deoxy-L-ribose was demonstrated.[4] Using the corresponding dihydroxyacetone derivative 2,2-dimethyl-1,3-dioxane-5-one,[5] the Enders group has previously synthesized a series of natural and unnatural deoxyketoses[6] and aza-sugars.[7] The enantioselective synthesis of all diastereomers of the 2-deoxypentoses and the 2,6-dideoxyhexoses from **1** has been accomplished. The desired enantiomer is available by choosing either RAMP or SAMP as the chiral auxiliary.

All diastereomers of the 2,6-dideoxyhexoses[8] are all found in nature in medicinally interesting glycosides.[9] Olivose and oliose are found in olivomycin,[10] chromomycin,[11] and plicamycin.[12] Digitoxose are found in the digitalis glycosides.[13] Boivinose are found in steroidic glycosides like stroboside[14] and corchoroside A.[15] The syntheses described below take advantage of **1**, where the C_3-part furnishes 1,2,3-trihydroxy units with each carbon representing stereogenic centers in all 2,6-dideoxyhexoses. Full control of the stereochemistry is demonstrated by the synthesis of all possible diastereomers.

Results and Discussion

Asymmetric α-alkylation of the C_s-symmetric **1** or the corresponding ketone presented a considerable challenge, because the reaction would have to show both regioselectivity and *cis*/*trans*-selectivity. The problem was overcome when it turned out that the diastereomer **2**, the RAMP-hydrazone of **1**, was formed exclusively upon extended storing of the hydrazone mixture at 4 °C (Scheme 1).[16] Alkylation of the hydrazone **2** with allyl bromide and methyl iodide gave the diastereomers **3** and **4**, respectively. The regioselectivity is presumably due to a directing of *t*BuLi by the methoxy group. Substitution at the equatorial position with high selectivity was observed. A second alkylation gave axial substitution at the opposite side, affording **5** or **6**. Formation of the hydrazone and the alkylations proceeded with high purity, and close to quantitative yield, therefore no purification was necessary for the first three steps.



Scheme 1. a) RAMP, $MgSO_4$, benzene, reflux; b) *t*BuLi, allyl bromide or MeI, THF, −100 °C; c) $NH_4H_2PO_4$, H_2O, THF; d) $NaBH_4$, H_2O, THF.

Conversion of the hydrazones to the corresponding ketones represented a problem. With the RAMP hydrazones this transformation is usually performed by ozonolysis. However, the olefin moieties in **5** and **6** are incompatible with ozone. Similarly, acidic hydrolysis of the hydrazone would also result in hydrolysis of the acetal function. Generation of the ketones **7** and **8** was, however, achieved in

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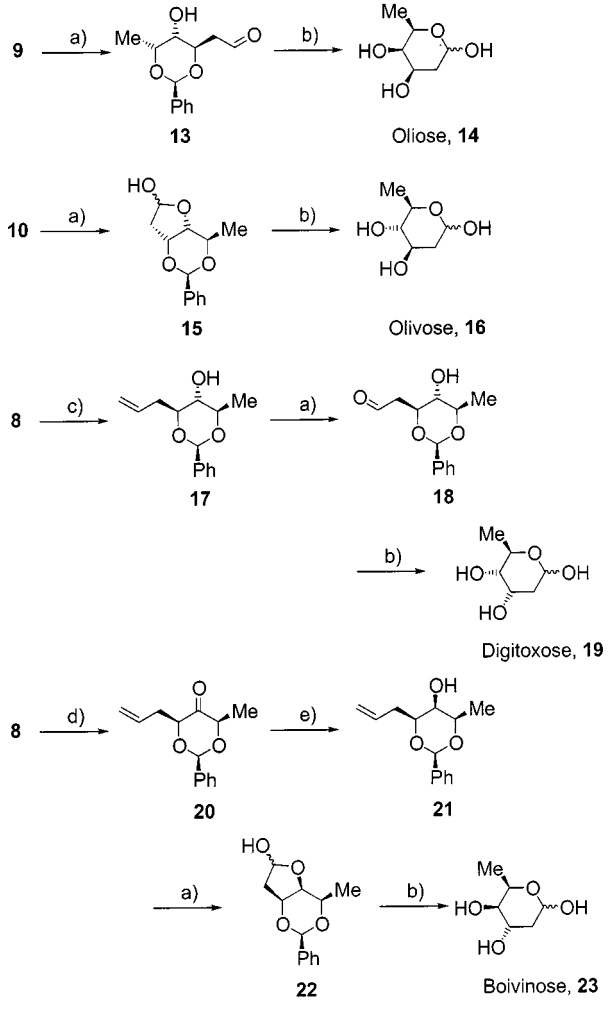
good yields upon treatment of **5** and **6** with aqueous ammonium dihydrogen phosphate. The spectroscopic properties were in agreement with the proposed structures. The elemental analysis of **8** was not accurate, due to the formation of undefined hydrates.

Reduction of **7** and **8** with $NaBH_4$ gave the equatorial alcohols with high selectivity, affording a 30:1 mixture of **9** and **11**, and a 12:1 mixture of **10** and **12**, respectively. Ozonolysis of **9** gave the aldose **13** (Scheme 2), whereas **10** gave the furanose **15**. In general, when the hydroxy and the allyl groups were in a *trans*-orientation on the 1,3-dioxan, the aldose form was obtained upon ozonolysis, whereas when they were *cis*-substituted, the furanose form was obtained. Hydrolysis of **13** and **15** gave the 2,6-dideoxyhexoses oliose **14** and olivose **16**, respectively.

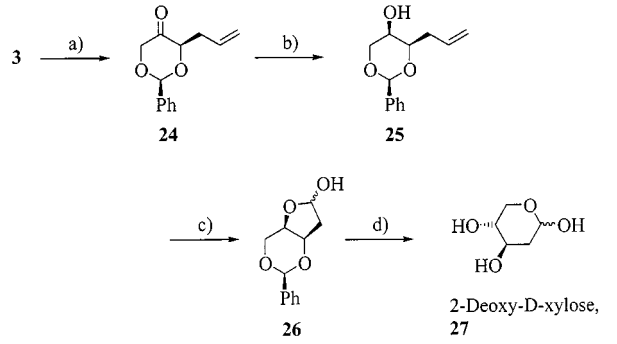


Scheme 2. Synthesis of the deoxyhexoses. a) O_3, MeOH, −78 °C; b) TFA, H_2O, THF; c) 25% NH_4OH − THF (4:1), then NA BH_4; d) 25% NH_4OH − THF (4:1) e) L-Selectride, THF, −78 °C.

Treatment of **8** with 25% ammonium hydroxide afforded epimerization of the di-equatorially α,α′-substituted **20**, obtained as a 30:1 mixture with **8** in 96% yield. Purification of the product by flash chromatography led to some loss of product, ascribed to hydrate formation. It was observed that whereas BDHA and its equatorially substituted derivatives easily formed hydrates upon exposure to water, the axially substituted derivatives retained the ketone. The ^{13}C NMR did not indicate a difference in electron density around the carbonyl carbon. Hence, the suppression of hydrate formation in the axially substituted derivatives is explained by steric arguments. Molecular mechanics and NOE studies have shown the carbonyl part of BDHA and its α-substituted derivatives to be flattened. Formation of the hydrate leads to a more distinct chair conformation of the dioxane rings as the C5 becomes sp^3 hybridized, implying that the axial 4- and 6-substituents are directed more axially. Thus, bulky axial substituents may suppress hydrate formation because a more distinct chair conformation would lead to a comparatively larger 1,3-strain.

When compound **8** was treated with ammonium hydroxide and $NaBH_4$ was added directly to the cold epimerization mixture, **17** was obtained with 4−5:1 selectivity over **21**. Chromatographic separation yielded 60% of **17** and 14% of **21**. Ozonolysis of **17** gave aldose **18**, which upon hydrolysis afforded digitoxose (**19**). Reduction of **20** by L-Selectride gave the axial alcohol **21** with 18:1 selectivity over **17**. Ozonolysis of **21** gave furanose **22**. Hydrolysis of **22** afforded boivinose (**23**), and completed the synthesis of all diastereomers of the 2,6-dideoxyhexoses.

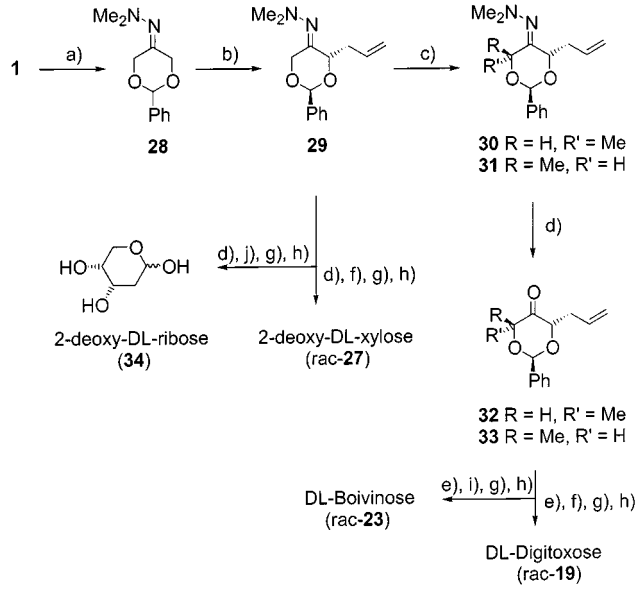
Reduction of **24** with L-Selectride gave the axial alcohol **25**, with no trace of the equatorial alcohol detectable by GC or NMR (Scheme 3). Ozonolysis and hydrolysis afforded 2-deoxy-D-xylose (**27**). Together with the recently reported synthesis of 2-deoxy-L-ribose from **3**,[4] this completes the synthesis of all diastereomers of all 2-deoxyriboses and 2,6-dideoxyhexoses from BDHA by similar strategies. The remaining enantiomers are available by choosing SAMP instead of RAMP as the chiral auxiliary.



Scheme 3: Synthesis of the 2-deoxy-D-xylose. a) $NH_4H_2PO_4$, H_2O, THF; b) L-Selectride, THF, −78 °C; c) O_3, MeOH, −78 °C; d) TFA, H_2O, THF.

By employing the dimethyl hydrazone **28** (Scheme 4) some of the racemic sugars were obtained. The intermediates were used as references for determination of the enantiomeric purities in the asymmetric syntheses. Alkylation of **28** with allyl bromide gave the axially substituted **29**, from which racemic 2-deoxyribose (**34**) and 2-deoxyxylose (*rac*-**27**) were obtained.[2] Alkylation of **29** with methyl iod-

ide gave a 4:1 mixture of **30** and **31**. Subsequent hydrolysis, epimerization, reduction, ozonolysis, and deprotection afforded the racemic compounds **17**−**23**, including digitoxose and boivinose.



Scheme 4. Synthesis of racemic deoxysugars. a) Me_2NNH_2, $MgSO_4$, toluene; b) *t*BuLi, allyl bromide, THF, −78 °C; c) *tBu*Li, MeI, THF, −78 °C; d) $NH_4H_2PO_4$, H_2O, THF; e) 25% NH_4OH − THF (4:1) f) $NaBH_4$, H_2O, THF g) O_3, MeOH, −78 °C; h) TFA, H_2O, THF; i) L-Selectride, THF, −78 °C; j) 25% NH_4OH − THF (4:1), then $NaBH_4$.

Conclusion

Any enantiomer of any diastereomer of the 2-deoxypentoses or the 2,6-dideoxyhexoses may be obtained from BDHA or **1** by the routes described above, by choosing either RAMP or SAMP as the chiral auxiliary. Hence, complete control of the stereochemistry at the three carbons during the formation of 1,2,3-trihydroxy moieties from BDHA was demonstrated.

Experimental Section

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 300 or DPX 400. − IR spectra were obtained from a Nicolet 200-SXC FT-IR spectrometer or a Perkin−Elmer 1420 IR spectrometer. − Mass spectra were recorded on an AEI MS-902 spectrometer at 70 eV (IP) and 180. Optical rotations were measured on a Perkin−Elmer 241 polarimeter. − GC analyses were performed on a Chrompack CP 9000 gas chromatograph equipped with a 12.5 m CP-Sil 5CB column. Chiral GC analysis were performed on a Carlo−Erba GC 8000 equipped with a CP Chirasil-dex CB fused silica WCOT column (25 m × 0.25 mm).

General Procedure I. − Alkylation of the RAMP-Hydrazone: To a stirred solution of **2** (290 mg, 1.0 mmol) in THF (5 mL) at −100 °C was added dropwise *t*BuLi (1.5 M in pentane, 1.1 mmol), and the temperature was maintained between −100 and −78 °C for 3 h. The temperature was lowered to −100 °C and the alkylating agent (1.2 mmol) was added. The temperature was kept below −90 °C for 2 h, and then allowed to slowly reach room temperature (> ca. 15 h). The reaction mixture was added Et_2O (30 mL), and the organic phase was washed with pH 7 buffer solution (2 × 3.5 mL) and brine (2 × 3.5 mL), dried ($MgSO_4$), and concentrated under reduced pressure to give the crude product as a pale yellow/orange oil. The product was subjected to flash chromatography [SiO_2, Et_2O/cyclohexane, 1:2 (**3** and **4**) or 1:6 (**5** and **6**)] prior to characterization. The crude products were in most cases used directly in the next reaction.

(*E*)-(2*R*,2′*S*,4′*R*)-(−)-1-(4-Allyl-2-phenyl-1,3-dioxan-5-ylideneamino)-2-(methoxymethyl)pyrrolidine (3): Starting with hydrazone **2** (0.51−5.32 mmol) and allyl bromide as the alkylation agent, the general procedure I gave crude **3** as a yellow oil in 95−100% yield, 93−98% pure (GC), and 85−96% *de* − $[\alpha]_D^{20}$ = −188 (*c* = 3.25, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.59−1.72 (m, 1 H, H-3), 1.85 (m, 2 H, 2 H-4), 2.01 (m, 1 H, H-3), 2.50−2.64 (m, 2 H, H-5, H-1′′), 2.77 (m, 1 H, H-1′′), 3.10 (dt, *J* = 9.4, 6.4 Hz, 1 H, H-5), 3.27−3.42 (m, 2 H, H-1′′′, H-2), 3.37 (s, 3 H, H-3′′′), 3.46 (dd, *J* = 8.3, 3.5 Hz, 1 H, H-1′′′), 4.62 (d, *J* = 15.4 Hz, 1 H, H-6′$_{ax}$), 4.63 (ddd, *J* = 7.3, 4.8, 1.1 Hz, 1 H, H-4′), 4.75 (dd, *J* = 15.4, 1.1 Hz, 1 H, H-6′$_{eq}$), 5.10 (dm, *J* = 10.2 Hz, 1 H, H-(*E*)-3′′), 5.16 (dm, *J* = 17.2, 1 H, H-(*Z*)-3′′), 5.76 (s, 1 H, H-2′), 6.00 (ddt*, *J* = 17.2, 10.2, 7.0 Hz, 1 H, H-2′′), 7.33−7.41 (m, 3 H, Ph), 7.48−7.53 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 22.9 (C-4), 26.8 (C-3), 38.3 (C-1′′), 56.0 (C-5), 59.2, 64.8 (C-6′), 66.7, 75.4 (C-2′′), 78.0 (C-4′), 98.8 (C-2′), 117.2 (C-3′′), 126.2 (Ph), 128.3 (Ph), 128.9 (Ph), 134.4 (C-2′′), 138.1 (Ph), 156.4 (C-5′). − IR (neat): $\tilde{\nu}$ = 2974, 2922, 2873, 2830, 1453, 1395, 1116, 1073, 1029, 915, 748, 698 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 331 (0.7), 330 (3.4 [M$^+$], 287 (2), 286 (13), 285 (69), 224 (3), 184 (11), 183 (82), 179 (39), 147 (11), 146 (100), 114 (15), 107 (13), 106 (46), 105 (70), 82 (12), 80 (15), 78 (10), 77 (45). −HRMS calcd. for $C_{19}H_{26}N_2O_3$: 330.1943. Found M$^+$ 330.1939.

(*E*)-(2*R*,2′*S*,4′*R*)-(−)-1-(4-Methyl-2-phenyl-1,3-dioxan-5-ylideneamino)-2-(methoxymethyl)pyrrolidine (4): Starting with hydrazone **2** (3.10−4.19 mmol) and methyl iodide as alkylation agent, the general procedure I gave crude **4** as an orange oil in 95−99% yield, 97−98% pure (GC) with 80−86% *de* (^{13}C NMR). − $[\alpha]_D^{20}$ = −38 (*c* = 1, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52 (d, *J* = 6.5 Hz, 3 H, Me), 1.60−1.71 (m, 1 H, H-3), 1.81−1.91 (m, 2 H, 2 H-4), 1.96−2.06 (m, 1 H, H-3), 2.64 (dt, *J* = 9.4, 7.9 Hz, 1 H, H-5), 3.11 (dt, *J* = 9.5, 6.3 Hz, 1 H, H-5), 3.25−3.33 (m, 2 H, H-1′′, H-2), 3.37 (s, 3 H, OMe), 3.41−3.49 (m, 1 H, H-1′′), 4.53 (d, *J* = 15.1 Hz, 1 H, H-6′), 4.68 (qd, *J* = 6.5, 0.9 Hz, 1 H, H-4′), 4.89 (dd, *J* = 15.1, 0.9 Hz, 1 H, H-6′), 5.79 (s, 1 H, H-2′), 7.34−7.42 (m, 3 H, Ph), 7.50−7.54 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 18.9 (Me), 22.9 (C-4), 26.9 (C-3), 56.1 (C-5), 64.5(C-6), 66.7(C-4), 75.1, 75.5, 99.5 (C-2′), 126.3 (Ph), 128.5 (Ph), 129.1 (Ph), 138.2 (Ph), 158.5 (C-5′). − IR (neat): $\tilde{\nu}$ = 2976, 2935, 2873, 2830, 1127, 1088, 1072, 1031, 698 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 305 (1.6), 304 (8) [M$^+$], 273 (3), 260 (16), 259 (90), 198 (5), 173 (6), 160 (14), 153 (38), 147 (11), 146 (100), 107 (12), 106 (44), 105 (65), 91 (10), 79 (10), 77 (49).

(2*R*,2′*S*,4′*R*,6′*R*)-(−)-1-(6-Allyl-4-methyl-2-phenyl-1,3-dioxan-5-ylideneamino)-2-(methoxymethyl)pyrrolidine (5): Starting with the crude **3** (0.32−2.51 mmol), with neat methyl iodide as the alkylating agent, the general procedure I gave **5** as an orange oil in 99% yield, 88−92% pure (GC) and 87−95% *de* Purification of the product by flash chromatography (SiO_2, Et_2O/cyclohexane, 1:20) yielded **32** in 63% yield as a pale yellow oil. $[\alpha]_D^{20}$ = −101 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56 (d, *J* = 7.0 Hz,

3 H, Me), 1.60−1.71 (m, 1 H, H-3), 1.80−1.90 (m, 2 H, 2 H-4), 1.97−2.09 (m, 1 H, H-3), 2.49−2.60 (m, 2 H, H-5, H-1′′), 2.81−2.91 (m, 1 H, H-1′′), 3.13 (dt, J = 9.3, 6.0 Hz, 1 H, H-5), 3.19−3.31 (m, 2 H, 2 H-1′′′), 3.35−3.41 (m, 1 H, H-2), 3.35 (s, 3 H, OMe), 4.65 (ddd, J = 7.8, 4.1. 0.9 Hz, 1 H, H-4′), 5.10 (dm, J = 10.2 Hz, 1 H, H-(*E*)-3′′), 5.18 (dm, J = 17.1 Hz, 1 H, H-(*Z*)-3′′), 5.21 (q, J = 6.9 Hz, 1 H, H-6′), 6.01 (s, 1 H, H-2′), 6.02 (ddt*, J = 17.2, 10.2, 6.0 Hz, 1 H, H-2′′), 7.33−7.42 (m, 3 H, Ph), 7.49−7.54 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 15.6 (Me), 22.7 (C-4), 26.8 (C-3), 35.9 (C-1′′), 55.3 (C-5), 59.3 (MeO), 66.8 (C-1), 69.9 (C-6′), 75.6 (C-1′′′), 76.1 (C-4′), 94.7 (C-2′), 117.1 (C-3′′), 126.4 (Ph), 128.4 (Ph), 129.0 (Ph), 135.3 (C-2′′), 138.4 (Ph), 161.7 (C-5′). − IR (neat): $\tilde{\nu}$ = 2975, 2927, 2872, 2829, 1127, 1087, 1027, 698 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 344 (3.88) [M$^+$] 343 (1), 300 (12), 299 (59), 238 (7), 198 (12), 197 (100), 194 (5), 193 (36), 186 (30), 161 (11), 160 (94), 125 (30), 123 (6), 114 (46), 113 (9), 108 (9), 107 (77), 106 (23), 105 (44), 82 (17), 80 (38), 79 (42), 77 (40).

(2*R*,2′*R*,4′*R*,6′*R*)-(+)-1-(4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-ylideneamino)-2-(methoxymethyl)pyrrolidine (6): Starting with the crude **4** in 1.67−3.35 mmol scale, with neat allyl bromide as electrophile, the general procedure I yielded **6** as a yellow solid in 95−98% yield, 96% pure (GC), with 83−88% *de* (^{13}C NMR). − $[\alpha]_D^{20}$ = + 122 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50 (d, 3 H, J = 6.2; Me), 1.58−1.68 (m, 1 H, H-3), 1.80−1.90 (m, 2 H, 2 H-4), 1.98−2.10 (m, 1 H, H-3), 2.51−2.66 (m, 2 H, H-1′′, H-5), 2.77−2.88 (m, 1 H, H-1′′), 3.13−3.42 (m, 4 H, H-5, H-2, 2 H-1′′′), 3.35 (s, 3 H, MeO), 4.75 (q, J = 6.1 Hz, 1 H, H-6′), 5.10 (dd, J = 10.2, 3.9 Hz, 1 H, H-4′), 5.15 (dm, J = 10.5 Hz, 1 H, H-(*E*)-3′′), 5.20 (dm, J = 17.2 Hz, 1 H, H-(*Z*)-3′′), 5.93 (ddt*, J = 17.1, 10.1, 6.9 Hz, 1 H, H-2′′), 6.03 (s, 1 H, H-2′), 7.33−7.41 (m, 3 H, Ph), 7.49−7.54 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 17.6 (Me), 22.9 (C-4), 27.1 (C-3), 33.3 (C-1′′), 55.3 (C-5), 59.2 (MeO), 66.7 (C-2), 73.0 (C-4), 73.4 (C-6), 76.0 (C-1′′′), 94.9 (C-2′), 117.7 (C-3′′), 126.4 (Ph), 128.5 (Ph), 129.0 (Ph), 134.4 (C-2′′), 138.3 (Ph), 160.8 (C-5′). − IR (KBr): $\tilde{\nu}$ = 1126, 1097, 1071, 1034, 968, 914, 748, 698 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 345 (1), 344 (8) [M$^+$], 343 (1), 313 (1), 300 (14), 299 (100), 238 (6), 198 (7), 197 (62), 193 (31), 186 (25), 160 (59), 148 (21), 125 (12), 120 (11), 114 (28), 66 (107), 106 (55), 105 (87), 91 (21), 90 (13), 83 (15), 82 (14), 80 (34), 79 (25), 78 (19), 77 (63).

General Procedure II. − Regeneration of Ketones from Hydrazones: To a solution of the hydrazone (1.0 mmol) in THF (6 mL) was added 1.6 M aqueous $NH_4H_2PO_4$ buffer solution (28 mL). The reaction mixture was stirred vigorously at room temperature. Upon complete conversion (typically 3−48 h), the reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL). If no hydrazone was detected, the extract was dried ($MgSO_4$) and concentrated under reduced pressure. Otherwise, the extract was concentrated, the residue was dissolved in THF and $NH_4H_2PO_4$ buffer as above, and the procedure was repeated.

(2*S*,4*R*)-(+)-4-Allyl-2-phenyl-1,3-dioxan-5-one (24): The hydrazone **3** (397 mg, 1.20 mmol) was hydrolyzed according to the general procedure II for 7 + 1 h to give 254 mg (97%) of a yellow solid of a mixture of **24** and the corresponding axially substituted ketone in 10:1 ratio (GC). Further reactions were performed on the crude material. For characterization, **24** was subject to flash chromatography (SiO_2, Et_2O/cyclohexane, 1:4), yielding the product as white needles. − $[\alpha]_D^{20}$ = +31 (*c* = 1.5, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.59 (m, 1 H, H-1′), 2.76 (m, 1 H, H-1′), 4.45 (m, 2 H, 2 H-6), 4.52 (dd, J = 7.2, 4.2 Hz, 1 H, H-4), 5.14 (dm, J = 10.2 Hz, 1 H, H-(*E*)-3′), 5.20 (dm, J = 17.2, Hz, 1 H, H-(*Z*)-3′), 5.93 (ddt*, J = 17.1, 10.2, 6.9 Hz, 1 H, H-2′), 5.96 (s, 1 H, H-2), 7.38−7.44 (m, 3 H, Ph), 7.51−7.56 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 34.2 (C-1′), 72.2 (C-6), 82.4 (C-4), 99.3 (C-2), 118 (C-3′), 126.1 (Ph), 128.4 (Ph), 129.3 (Ph), 132.9, 137.0, 205.3 (C-5). − IR (neat): 3074, 2867, 2832, 1738, 1396, 1125, 1029, 991, 920, 759, 699 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 219 (0.58), 218 (2.62) [M$^+$], 178 (3), 177 (30), 149 (10), 148 (91), 120 (50), 119 (44), 107 (24), 106 (44), 105 (100), 92 (37), 91 (44), 90 (45), 89 (24), 82 (12), 79 (15), 78 (10), 77 (47).

(2*S*,4*R*,6*R*)-(+)-4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-one (7): The hydrazone **5** (803 mg, 2.33 mmol) was hydrolyzed according to the general procedure II for 48 + 24 h to give 557 mg (103%) of a dark orange liquid. Purification by flash chromatography (SiO_2, Et_2O/cyclohexane, 1:20) gave 354 mg (65%) of **7** as a pale yellow liquid. $[\alpha]_D^{20}$ = + 182 (*c* = 1.2, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.9 Hz, 3 H, Me), 2.56 (m, 1 H, H-2′), 2.77 (m, 1 H, H-2′), 4.45 (qd, J = 6.9, 1.3 Hz, 1 H, H-6), 4.51 (ddd, J = 7.6, 4.2, 1.2 Hz, 1 H, H-4), 5.16 (dm, J = 10.2, 1 H, H-(*E*)-3′), 5.22 [d(q), J = 17.2, 1.5 Hz, 1 H, H-(*Z*)-3′], 5.95 (ddt*, J = 17.1, 10.2, 6.9 Hz, 1 H, H-2′), 6.07 (s, 1 H, H-2), 7.39−7.47 (m, 3 H, Ph), 7.54−7.58 (m, 2 H, Ph). − NOE experiments: irr. at H-2 → NOE at H-4; irr. at Me → NOE at H-6 and at H-2. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 15.2 (Me), 34.3 (C-1′), 66.0 (C-6), 79.5 (C-4), 97.4 (C-2), 118.4 (C-3′), 126.3 (Ph), 128.6 (Ph), 129.2 (Ph), 133.2 (C-2′), 138.1 (Ph), 209.8 (C-5). − IR (neat): $\tilde{\nu}$ = 3077, 3035, 2984, 2938, 2870, 1749, 1643, 1452, 1431, 1295, 1210, 1127, 1029, 998, 921 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 233 (0.1), 232) [0.8 M$^+$], 231 (0.8), 191 (4), 189 (3), 188 (22), 178 (6), 162 (11), 160 (17), 134 (24), 133 (17), 107 (35), 106 (28), 105 (100), 104 (20), 91 (18), 90 (43), 89 (18), 82 (95), 79 (15), 78 (16), 77 (42). − $C_{14}H_{16}O_3 \cdot 1/2H_2O$: calcd. C 69.69, H 7.10; found C 68.97, H 7.14.

(2*R*,4*R*,6*R*)-(+)-4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-one (8): The hydrazone **6** (402 mg, 1.17 mmol) was hydrolyzed according to the general procedure II for 48 + 24 h to give quantitative yield of the crude product as an orange liquid. Flash chromatography of the crude product (SiO_2, Et_2O/cyclohexane, 1:20) yielded 209 mg (77%) of **8** as a colorless liquid. $[\alpha]_D^{20}$ = + 217 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, J = 6.8 Hz, 3 H, Me), 2.49−2.70 (m, 2 H, 2 H-1′), 4.42 (ddd, J = 8.2, 4.5, 1.1, 1 H, H-4), 4.54 (qd, J = 6.8, 1.2 Hz, 1 H, H-6), 5.10−5.20 (m, 2 H, 2 H-3′), 5.85 (ddt*, J = 17.1, 10.2, 6.9 Hz, 1 H, H-2′), 6.12 (s, 1 H, H-2), 7.37−7.45 (m, 3 H, Ph), 7.53-7-57 (m, 2 H, Ph). − NOE experiments: irr. at H-2 → NOE at H-6, H-1′ and Ph; irr. at Me → NOE at H-6; irr. at H-1′ → NOE at H-4, H-2′, H-(*Z*)-3′ and H-2; irr. at H-6 → NOE at H-2 and Me; irr. at H-4 → NOE at H-1′ and H-2′. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 15.2 (Me), 34.3 (C-1′), 76.0 (C-4), 76.5 (C-6), 97.5 (C-2), 118.4 (C-3′), 126.3 (Ph), 128.6 (Ph), 129.2 (Ph), 133.3 (C-2′), 137.9 (Ph), 209.5 (C-5). − IR (neat): $\tilde{\nu}$ = 2985, 2868, 1747, 1642, 1451, 1371, 1292, 1211, 1125 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 232 (0.9) [M$^+$], 192 (0.9), 191 (5), 188 (3), 163 (8), 162 (48), 160 (6), 135 (5), 134 (51), 133 (24), 119 (6), 118 (5), 107 (33), 106 (68), 105 (100), 104 (12), 91 (15), 90 (38), 89 (13), 82 (31), 79 (13), 78 (12), 77 (75).

(2*S,4*S**,6*R**)-4-Allyl-6-methyl-2-phenyl-1,3-dioxane-5-one (32):** The dimethylhydrazones **30** and **31** in 4.9:1 ratio (404 mg, 1.47 mmol) was hydrolyzed according to the general procedure II for 16 h to give 347 mg (100%) of pale yellow liquid, containing 84% **32** and 16% **33** (by GC). Compound **30** (84%): − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, J = 7.0 Hz, 3 H, Me), 2.64−2.71 (m, 2 H, 2 H-1′), 4.47 (t, J = 6.7 Hz, 1 H, H-4), 4.52 (q, J = 6.9 Hz, 1 H, H-6), 5.17 (dm, J = 10 Hz, 1 H, H-(*E*)-3′), 5.21 (dm, J = 17 Hz, 1 H, H-(*Z*)-3′), 5.89 (ddt, J = 17.1, 10.2, 6.9 Hz, 1 H, H-2′), 6.16 (s, 1 H, H-2), 7.38−7.47 (m, 3 H, Ph), 7.52−7.58 (m,

2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 15.2 (Me), 34.3 (C-1′), 74.4 (C-6), 77.8 (C-4), 93.9 (C-2), 118.2 (C-3′), 126.1 (Ph), 128.4 (Ph), 128.9 (Ph), 133.1 (C-2′), 137.5 (Ph), 209.1 (C-5).

General Procedure III. − α-Epimerization: To a solution of the axially α-substituted ketone (1.0 mmol) in THF (9 mL) was added aqueous NH_3 (28%, 30 mL), and the mixture was stirred vigorously for 9 h at room temperature, then for 12 h at 0. The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The extract was dried ($MgSO_4$) and concentrated under reduced pressure.

(2*R*,4*S*,6*R*)-4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-one (20): A solution of **8** (254 mg, 1.09 mmol) was epimerized as described the general procedure III to give **20** as a yellow solid (244 mg, 96%, 30:1 mixture with **8**). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (d, *J* = 6.6 Hz, 3 H, Me), 2.54−2.66 (m, 1 H, H-1′), 2.72−2.81 (m, 1 H, H-1′), 4.50−4.60 (m, 2 H, H-4, H-6), 5.14 (dm, *J* = 10.2 Hz, 1 H, H-(*E*)-3′), 5.21 (dm, *J* = 17.3 Hz, 1 H, H-(*Z*)-3′), 5.94 (ddt*, *J* = 17.2, 10.2, 6.9 Hz, 1 H, H-2′), 6.02 (s, 1 H, H-2), 7.33−7.48 (m, 3 H, Ph), 7.49−7.62 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 15.7 (Me), 34.7 (C-1′), 80.1 (C-4), 83.0 (C-6), 99.9 (C-2), 118.2 (C-3′), 126.4 (Ph), 128.5 (Ph), 129.4 (Ph), 133.5 (C-2′), 137.4 (Ph), 206.1 (C-5). − IR (neat): $\tilde{\nu}$ = 2986, 2836, 1735, 1134, 1048, 1030, 757, 698 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 233 (0.5), 232 (3) [M^+], 231 (2), 192 (4), 191 (31), 189 (3), 188 (12), 162 (55), 160 (13), 134 (66), 133 (27), 107 (51), 106 (28), 105 (100), 104 (19), 91 (23), 90 (62), 89 (18), 83 (11), 82 (96), 79 (17), 78 (12), 77 (48).

General Procedure IV. − Reduction with $NaBH_4$: To a stirred solution of the ketone (1.0 mmol) in THF (7 mL) and water (28 mL) at 0 °C was added $NaBH_4$ (75 mg, 2 mmol). After 30 min the mixture was allowed to reach room temperature, and was extracted with CH_2Cl_2 (5 × 10 mL). The organic phase was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure.

General Procedure V. − Epimerization and Reduction with $NaBH_4$: To a stirred solution of the ketone (1.0 mmol) in THF (8 mL) was added 25% aqueous NH_3 (32 mL), and the mixture stirred at room temperature for 4 h. The temperature was lowered to 0 °C, the reaction mixture was stirred for another 4 h, and $NaBH_4$ (75 mg, 2 mmol) was added. The temperature was allowed to reach room temperature, and the mixture was extracted with CH_2Cl_2 (5 × 10 mL). The extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure.

General Procedure VI. − Reduction with L-Selectride: To a stirred solution of the ketone (1.0 mmol) in THF (4 mL) at −78 was added dropwise to a solution of lithium tri(*sec*-butyl)borohydride (L-Selectride®) in THF (1.0 M, 1.8 mL, 1.8 mmol). The reaction mixture was slowly allowed to reach room temperature. The product mixture was cooled on an ice/water-bath, and residual hydride was quenched with water (0.25 mL). Ethanol (1.0 mL), 2.5 M NaOH (1.5 mL), and 35% H_2O_2 (1.0 mL) was added. Diethyl ether (20 mL) was added, and the organic phase was washed with buffer solution (pH 7, 4 × 3 mL) and brine (3 mL), dried ($MgSO_4$), and concentrated under reduced pressure.

(2*S*,4*R*,5*R*)-(+)-4-Allyl-2-phenyl-1,3-dioxan-5-ol (25): Reduction of **24** (578 mg, 2.69 mmol) according to the general procedure VI yielded the crude product as 564 mg of a yellow oil, consisting of **25**. Purification by flash chromatography afforded 442 mg (75%, > 97% *ee* (chiral GC)) of **25** as a colorless oil. No trace of the equatorial alcohol was detected (> 100:1 in favor of **25**). − **Compound 25:** $[\alpha]_D^{20}$ = +27 (*c* = 1, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42−2.53 (m, 2 H, H-1′), 2.65 (d, *J* = 10.6 Hz, 1 H, OH), 3.50 (d, *J* = 9.3 Hz, 1 H, H-5), 3.91 (td, *J* = 7.1, 1.2 Hz, 1 H, H-4), 4.04 (dd, *J* = 11.8, 1.4 Hz, 1 H, H-6_{ax}), 4.23 (dd, *J* = 11.8, 2.0 Hz, 1 H, H-6_{eq}), 5.12 (dm, *J* = 10.2 Hz, 1 H, H-(*E*)-3′), 5.20 (dm, *J* = 17.1 Hz, 1 H, H-(*Z*)-3′), 5.56 (s, 1 H, H-2), 5.86 (ddt*, *J* = 17.2, 10.2, 7.5, 6.8 Hz, 1 H, H-2), 7.33−7.40 (m, 3 H, Ph), 7.47−7.52 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 35.6 (C-1′), 64.8 (C-5), 72.8 (C-6), 79.7 (C-4), 101.4 (C-2), 118.0 (C-3′), 125.9 (Ph), 128.3 (Ph), 129.0 (Ph), 133.4 (C-2′), 137.9 (Ph). − IR (neat): $\tilde{\nu}$ = 3436 (broad), 3070, 2977, 2916, 2856, 1642, 1452, 1399, 1360, 1215, 1156, 1091, 1028, 997, 918, 749, 699 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 220 (2) [M^+], 219 (7), 189 (1), 179 (17), 177 (3), 150 (6), 149 (5), 108 (7), 107 (100), 105 (40), 91 (22), 79 (58), 78 (10), 77 (45).

(2*S*,4*R*,5*S*,6*R*)-(−)-4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-ol (9): Reduction of **7** (244 mg, 1.05 mmol) according to the general procedure IV afforded 234 mg of white crystals (95% yield), 30:1 mixture of **9** and **11**, > 98% *ee* (chiral GC). The product was recrystallized from Et_2O and pentane prior to characterization. M.p. 85 °C. $[\alpha]_D^{20}$ = −77 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46 (d, *J* = 7.0 Hz, 3 H, Me), 1.85 (d, *J* = 2.6 Hz, 1 H, OH), 2.39−2.49 (m, 1 H, H-1′), 2.56−2.65 (m, 1 H, H-1′), 3.87−3.92 (m, 2 H, H-4, H-5), 4.42 (qd, *J* = 6.9, 5.0 Hz, 1 H, H-6), 5.14 (dm, *J* = 10.2 Hz, 1 H, H-3-*E*), 5.21 (ddd, *J* = 17.2, 3.3, 1.5 Hz, 1 H, H-3-*Z*), 5.84 (s, 1 H, H-2), 6.02 (ddt*, *J* = 17.2, 10.2, 7.0 Hz, 1 H, H-2), 7.31−7.43 (m, 3 H, Ph), 7.44−7.53 (m, 2 H, Ph). NOE experiments: irr. at Me → NOE at H-4/H-5, H-6 and H-2; irr. at H-2 → NOE at Me, H-4/H-5 and Ph; irr. at OH → NOE at H-4/H-5; irr. at H-6 → NOE at Me and H-4/H-5. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 11.8 (Me), 37.1 (C-1′), 69.0, 71.8 (C-6), 75.5, 93.9 (C-2), 117.7 (C-3′), 126.3 (Ph), 128.4 (Ph), 128.9 (Ph), 134.6 (C-2′), 138.5 (Ph). − IR (KBr): $\tilde{\nu}$ = 3410 (broad), 1120, 1095, 1067, 1045, 1032, 989, 966, 924, 912, 781, 702 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 235 (0.95), 234 (6.56) [M^+], 233 (8), 194 (1), 193 (10), 191 (1), 190 (4), 189 (3), 164 (4), 163 (8), 108 (9), 107 (100), 106 (7), 105 (29), 84 (30), 83 (13), 79 (23), 77 (18). − $C_{14}H_{18}O_3$: calcd. C 71.77, H 7.74; found C 71.87, H 7.62.

(2*R*,4*R*,5*R*,6*R*)-(+)-4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-ol (10): Reduction of **7** (160 mg, 0.69 mmol) by the general procedure IV gave 161 mg (100%) of a colorless, viscous oil, consisting of **10** and **12** in 12:1 ratio (determined by ^{1}H NMR). − $[\alpha]_D^{20}$ = + 55 (*c* = 1.0, $CHCl_3$). − ^{1}H NMR (MHz, $CDCl_3$): δ = 1.39 (d, *J* = 6.1 Hz, 3 H, Me), 1.94 (m, 1 H, OH), 2.51−2.62 (m, 1 H, H-1′), 2.73−2.86 (m, 1 H, H-1′), 3.79 (dt, *J* = 9.1, 5.6 Hz, 1 H, H-5), 3.97 (dq, *J* = 9.0, 6.1 Hz, 1 H, H-6), 4.28 (p, *J* = 5.2 Hz, 1 H, H-4), 5.15 (dm, *J* = 10.2 Hz, 1 H, H-(*E*)-3′), 5.22 (dm, *J* = 17.1 Hz, 1 H, H-(*Z*)-3′), 5.82 (s, 1 H, H-2), 5.94 (ddt*, *J* = 17.1, 10.2, 6.9 Hz, 1 H, H-2′), 7.32−7.41 (m, 3 H, Ph), 7.47−7.51 (m, 2 H, Ph). − ^{13}C NMR (MHz, $CDCl_3$): δ = 18.5 (Me), 30.0 (C-1′), 71.0 (C-5), 73.0 (C-6), 75.2 (C-4), 94.2 (C-2), 117.5 (C-3′), 126.3 (Ph), 128.5 (Ph), 129.0 (Ph), 134.9 (C-2′), 138.4 (Ph). − IR (neat): $\tilde{\nu}$ = 3457 (broad), 3071, 2977, 2932, 2883, 1642, 1451, 1398, 1376, 1307, 1215, 1149, 1075, 1028, 993, 914, 751, 699 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 235 (0.4), 234 (4), 233 (6), 194 (3), 193 (20), 190 (2), 164 (7), 163 (12), 108 (7), 107 (100), 106 (8), 105 (34), 79 (18), 77 (19). − $C_{14}H_{18}O_3$: calcd. C 71.77, H 7.74; found C 71.38; H 8.46.

(2*R*,4*R*,5*R*,6*R*)-4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-ol (17): Reduction of **8** (112 mg, 0.48 mmol) according to the general procedure V gave the crude product as 111 mg (98%) of a colorless oil, consisting of **17** and **21** in 4:1 ratio. Separation by flash chromatography (Et_2O/cyclohexane, 1:2) afforded 67 mg (60%) **17** as white crystals [86% *ee* (chiral GC)], together with 16 mg (14%) of **21**. − **Compound 17:** M.p. 47−52 °C (not recrystallized). − $[\alpha]_D^{20}$ = −13 (*c* = 1, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.41 (d, *J* =

6.2 Hz, 3 H, Me), 1.86 (d, J = 5.2 Hz, 1 H, OH), 2.43−2.53 (m, 1 H, H-1′), 2.59−2.69 (m, 1 H, H-1′), 3.23 (td, J = 9.0, 5.1 Hz, 1 H, H-5), 3.65 (ddd, J = 9.1, 6.8, 4.4 Hz, 1 H, H-4), 3.69 (dq, J = 9.0, 6.2 Hz, 1 H, H-6), 5.15 (dm, J = 10.2 Hz, 1 H, H-(*E*)-3′), 5.22 (dm, J = 17.3 Hz, 1 H, H-(*Z*)-3′), 5.58 (s, 1 H, H-2), 6.03 (ddt*, J = 17.2, 10.2, 7.1 Hz, 1 H, H-2), 7.34−7.42 (m, 3 H, Ph), 7.48−7.54 (m, 2 H, Ph). − NOE experiments: irr. at OH → NOE at H-5 and H-4/H-6; irr. at Me → NOE at H-4; irr. at H-2 → NOE at H-4/H-6 and Ph; irr. at H-5 → no NOE. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 18.2 (Me), 36.9 (H-1′), 72.1 (H-5), 77.4 (H-4/H-6), 80.4 (H-4/H-6), 100.6 (H-2), 117.7 (H-3′), 126.4 (Ph), 128.4 (Ph), 129.0 (Ph), 134.6 (H-2), 138.1 (Ph). − IR (neat): ṽ = 3466 (broad), 3072, 2977, 2856, 1409, 1091, 1050, 1029, 756, 698 cm^{-1}. − MS: *m*/*z* (% rel. int.) = 235 (0.5), 234 (5) [M$^+$], 233 (5), 207 (2), 194 (3), 193 (22), 164 (8), 108 (9), 107 (100), 105 (20), 84 (20), 79 (19), 77 (17). − $C_{13}H_{18}O_3$: calcd. C 71.77, H 7.74; found C 70.75, H 7.81.

(2*R*,4*S*,5*R*,6*R*)-(−)-4-Allyl-6-methyl-2-phenyl-1,3-dioxan-5-ol (21): Reduction of **20** (255 mg, 1.1 mmol) according to the general procedure VI yielded the crude product as 266 mg of a pale yellow oil (77% pure by GC), consisting of **21** and **17** in 19:1 ratio (determined by ^{1}H NMR). Purification by flash chromatography (SiO_2, Et_2O/cyclohexane, 1:2) afforded 174 mg (68%) of **21**: M.p. 40−43 °C(not recrystallized). − $[\alpha]_D^{20}$ = −30 (c = 1, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 (d, J = 6.4 Hz, 3 H, Me), 1.70 (d, J = 11.8 Hz, 1 H, OH), 2.45 (s, 1 H), 2.49−2.56 (m, 2 H, 2 H-1′), 3.32 (d, J = 11.4 Hz, 1 H, H-5), 3.87 (td, J = 7.1, 0.9 Hz, 1 H, H-4), 4.01 (qd, J = 6.4, 1.0 Hz, 1 H, H-6), 5.14 [dm, J = 10.1 Hz, 1 H, H-(*E*)-3′], 5.22 [dm, J = 17.1 Hz, 1 H, H-(*Z*)-3′], 5.61 (s, 1 H, H-2), 5.89 (ddt*, J = 17.1, 10.0, 7.1 Hz, 1 H, H-2′), 7.34−7.44 (m, 3 H, Ph), 7.50−7.55 (m, 2 H, Ph). − NOE experiments: irr. at H-2 → NOE at H-4 and H-6; irr. at H-6 → NOE at H-2 and Me; irr. at H-4 → NOE at H-2; irr. at H-5 → NOE at H-4, H-6 and Me; irr at OH → No NOE; irr. at Me → NOE at H-6. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 17.6 (Me), 36.0 (C-1′), 67.8 (C-5), 77.2 (C-6), 80.8 (C-4), 101.6 (C-2), 118.3 (C-3′), 126.4 (Ph), 128.7 (Ph), 129.4 (Ph), 134.0 (C-2′), 138.4 (Ph). − IR (neat): ṽ = 3306 (broad), 3070, 2982, 2863, 1641, 1403, 1337, 1172, 1098, 1069, 1028, 999, 749, 699 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 220 (2) [M$^+$], 219 (7), 189 (1), 179 (17), 177 (3), 150 (6), 149 (5), 108 (7), 107 (100), 105 (40), 91 (22), 79 (58), 78 (10), 77 (45).

General Procedure VII. − Ozonolysis: Through a solution of the alkene (1.0 mmol) in MeOH (30 mL) at −78 °C was passed a stream of ozone, until a persistent blue color appeared. The solution was flushed with N_2 until no more ozone was detected. After 30 min, Me_2S (0.7 mL) was added and the solution was allowed to slowly reach room temperature and stirred overnight. Concentration under reduced pressure gave the crude product, which was purified by flash-chromatography or crystallization.

3,5-*O*-Benzylidene-2-deoxy-DL-*erythro*-pentoaldose (26): Preparation from racemic **25** (55 mg, 0.25 mmol) as described in the general procedure VII. Purification of the crude product by flash chromatography (SiO_2, Et_2O/cyclohexane, 1:1; then EtOAc) gave **26** as a colorless oil (53 mg, 95%). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (d, J = 5.4 Hz, 1 H, OH), 2.86 (ddd, J = 16.9, 6.9, 2.1 Hz, 1 H, H-2), 2.94 (ddd, J = 16.9, 5.1, 1.6 Hz, 1 H, H-2), 3.58−3.71 (m, 2 H), 4.12 (ddd, J = 8.7, 6.9, 5.1, 1 H, H-3), 4.30 (m, 1 H, H-5), 5.52 (s, 1 H, benzylidene), 7.33−7.40 (m, 3 H, Ph), 7.42−7.49 (m, 2 H, Ph), 9.85 (t, J = 1.9, 1 H, H-1). − ^{13}C NMR (400 MHz, $CDCl_3$): δ = 46.5 (C-2), 65.4, 71.4, 77.0, 101.0 (benzylidene), 126.0 (Ph), 128.2 (Ph), 129.0 (Ph), 137.2 (Ph), 200.8 (C-1). − IR (neat): 3448 (broad), 2858, 1723, 1455, 1397, 1076, 1026, 757, 699 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 222 (13) [M$^+$], 221 (10), 150 (6), 149 (8), 108 (8), 107 (100), 106 (28), 105 (57), 91 (9), 79 (22), 77 (35).

3,5-*O*-Benzylidene-2-deoxy-D-*threo*-pentofuranose (26): Preparation from **25** (57 mg, 0.26 mmol) according to the general procedure VII. Purification by flash chromatography (SiO_2, Et_2O/cyclohexane, 1:1, then EtOAc) gave another 51 mg (89%) **26** as a crystalline solid. − $[\alpha]_D^{20}$ = +7 changing to −32 (equilibrium) (c = 1.0, $CHCl_3$). − ^{1}H and ^{13}C NMR showed the crystals to consist of essentially pure α-anomer, and the β-anomer to be in excess in an approximately 2:1 anomeric mixture at equilibrium in $CDCl_3$. **The α-Anomer (Crystalline):** M.p. 135−136 °C. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10 (dt, J = 14.6, 4.7 Hz, 1 H, H-2), 2.50 (dd, J = 14.6, 5.7 Hz, 1 H, H-2), 3.09 (d, J = 3.1 Hz, 1 H, OH), 4.07 (td, J = 2.2, 1.1 Hz, 1 H, H-4), 4.17 (dd, J = 13.2, 2.2 Hz, 1 H, H-5), 4.44 (d, J = 13.2 Hz, 1 H, H-5), 4.56 (dd, J = 5.0, 2.3 Hz, 1 H, H-3), 5.45 (s, 1 H, acetal), 5.88 (m, 1 H, H-1), 7.32−7.40 (m, 3 H, Ph), 7.46−7.50 (m, 2 H, Ph). − NOE experiments: irr. at H-1 → NOE at OH and H-2$_\alpha$; irr. at H-2$_\alpha$ → NOE at H-2$_\beta$ and H-1; irr. at H-2$_\beta$ → NOE at H-2$_\alpha$, H-4, and H-3. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 42.2 (C-2), 67.1 (C-5),72.8 (C-4), 76.1 (C-3), 98.9 (C-1), 99.4 (acetal), 126.1 (Ph), 128. 3 (Ph), 129.0 (Ph), 137.8 (Ph). − IR (KBr): ṽ = 3392 (broad), 3059, 2976, 2914, 1448, 1397, 1369, 1328, 1253, 1134, 1069, 1025, 992, 826, 743, 697 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 222 (3) [M$^+$], 221 (11), 176 (2), 175 (5), 150 (2), 149 (3), 108 (7), 107 (81), 106 (51), 105 (100), 91 (14), 81 (16), 79 (41), 78 (20), 77 (97). **The β-Anomer (Major Anomer at Equilibrium in $CDCl_3$):** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.16−2.31 (m, 2 H, 2 H-2), 3.82 (s, 1 H, OH), 3.85 (d, J = 12.6 Hz, 1 H, H-4), 4.16 (dm, J 13 Hz, 1 H, H-5), 4.52 (d, J = 13.5 Hz, 1 H, H-5), 4.58 (m, 1 H, H-3), 5.48 (s, 1 H, acetal), 5.49 (m, 1 H, H-1), 7.32−7.40 (m, 3 H, Ph), 7.46−7.50 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 41.7 (C-2), 67.9 (C-5), 74.8 (C-4), 77.3 (C-3), 99.7 (acetal), 99.8 (C-1), 126.0 (Ph), 128.5 (Ph), 129.3 (Ph), 137.5 (Ph).

(+)-3,5-*O*-Benzylidene-2,6-dideoxy-D-*lyxo*-hexoaldose (13): Preparation from **9** (164 mg, 0.70 mmol) as described by the general procedure VII. The crude product was purified by flash chromatography (SiO_2, EtOAc/cyclohexane, 1:1) to give (+)-**13** (151 mg, 91%) as a colorless syrup. $[\alpha]_D^{20}$ = +58 (c = 1.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, J = 7.0 Hz, 3 H, H-6), 2.38 (m, 1 H, OH), 2.79 (ddd, J = 16.8, 7.0, 2.1 Hz, 1 H, H-2), 2.90 (ddd, J = 16.8, 4.9, 1.5 Hz, 1 H, H-2), 3.86 (m, 1 H, H-4), 4.36−4.50 (m, 2 H, H-3 and H-5), 5.87 (s, 1 H, acetal), 7.35−7.41 (m, 3 H, Ph), 7.44−7.48 (m, 2 H, Ph), 9.85 (t, J = 1.7 Hz, 1 H, H-1). − ^{13}C NMR (300 MHz, $CDCl_3$): 11.4 (C-6), 46.9 (C-2), 68.7 (C-4), 71.2 (C-4/C-6), 72.3 (C-6/C-4), 93.9 (acetal), 126.3 (Ph), 128.5 (Ph), 129.2 (Ph), 137.9 (Ph), 201.2 (C-1). − IR (neat): ṽ = 3445 (broad), 1723, 1095, 1077 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 237 (1), 236 (4) [M$^+$], 235 (6), 174 (3), 163 (5), 151 (2), 133 (2), 123 (2), 113 (2), 108 (9), 107 (100), 106 (26), 105 (41), 86 (57), 79 (20), 77 (36). − $C_{13}H_{16}O_4$: calcd. C 66.09, H 6.83, O 27.09; found C 65.80, H 8.13, O 26.07.

(+)-3,5-O-Benzylidene-2,6-dideoxy-D-*arabino*-hexofuranose (15): Preparation from **10** (107 mg, 0.46 mmol) as described by the general procedure VII. Purification of the crude product by flash chromatography (SiO_2, EtOAc/cyclohexane, 1:1) yielded an anomeric mixture of **15** (101 mg, 94%) as a colorless oil. $[\alpha]_D^{20}$ = +48 (c = 1.2, $CHCl_3$). **Major Anomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.44 (d, J = 6.2 Hz, 3 H, H-6), 2.12−2.21 (m, 1 H, H-2), 2.33−2.43 (m, 1 H, H-2), 3.03 (dd, J = 3.3, 1.0 Hz, 1 H, OH), 3.81 (dq, J = 7.8, 6.3 Hz, 1 H, H-5), 4.06 (dd, J = 7.9, 5.8 Hz, 1 H, H-4), 4.71 (dt, J = 7.1, 6.0 Hz, 1 H, H-3), 5.68 (ddd, J = 5.3, 3.3, 2.0 Hz, 1 H, H-1), 5.85 (s, 1 H, acetal), 7.32−7.45 (m, 3 H, Ph), 7.46−7.55

(m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 19.8 (C-6), 37.9 (C-2), 71.8 (C-3), 73.0 (C-5), 79.5 (C-4), 96.7 (acetal), 98.3 (H-1), 126.6 (Ph), 128.7 (Ph), 129.3 (Ph), 138.7 (Ph). **Minor Anomer:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (d, *J* = 5.9 Hz, 3 H, H′-6), 2.12−2.21 (m, 1 H, H′-2), 2.26 (ddd, *J* = 14.2, 2.6, 1.4 Hz, 1 H, H′-2), 3.73 (d, *J* = 9.0 Hz, 1 H, OH′), 3.93−4.01 (m, 2 H, H′-4, H′-5), 4.41 (ddd, *J* = 6.0, 4.4, 2.6 Hz, 1 H, H′-3), 5.51 (ddd, *J* = 9.0, 4.8, 1.3 Hz, 1 H, H′-1), 6.00 (s, 1 H, acetal′), 7.32−7.45 (m, 3 H, Ph), 7.46−7.55 (m, 2 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 19.6 (C′-6), 38.9 (C′-2), 71.4 (C′-3), 74.0 (C′-5), 84.4 (C′-4), 97.5 (acetal′), 100.1 (H′-1), 126.6 (Ph′), 128.7 (Ph′), 129.3 (Ph′), 138.5 (Ph′). − **Both Anomers:** IR (neat): ṽ = 3424 (broad), 2975, 2932, 1452, 1379, 1306, 1292, 1211, 1130, 1064, 1030, 945, 756, 699 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 236 (1) [M$^+$], 235 (3), 234 (1), 218 (3), 189 (6), 163 (3), 123 (3), 113 (11), 107 (100), 106 (39), 105 (77), 86 (47), 79 (21), 78 (11), 77 (58). − $C_{13}H_{16}O_4$: calcd. C 66.09, H 6.83, O 27.09; found C 65.05, H 6.77, O 28.18.

3,5-*O*-Benzylidene-2,6-dideoxy-DL-*ribo*-hexose (18): Preparation from racemic **17** (61 mg, 0.26 mmol) as described by the general procedure VII. Purification of the crude product by flash chromatography (SiO_2, EtOAc/cyclohexane, 1:1) gave racemic **18** (60 mg, 98%) as a colorless oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, *J* = 6.2 Hz, 3 H, H-6), 2.53 (s (broad), 1 H, OH), 2.85 (ddd, *J* = 16.7, 6.9, 2.2 Hz, 1 H, H-2), 2.93 (ddd, *J* = 16.7, 5.0, 1.7 Hz, 1 H, H-2), 3.20 (t, *J* = 9.1 Hz, 1 H, H-4), 3.73 (dq, *J* = 8.9, 6.2 Hz, 1 H, H-5), 4.13 (ddd, *J* = 9.2, 6.9, 5.0 Hz, 1 H, H-3), 5.62 (s, 1 H, acetal), 7.34−7.41 (m, 3 H, Ph), 7.45−7.51 (m, 2 H, Ph), 9.85 (dd, *J* = 2.0, 1.9 Hz, 1 H, H-1). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 18.3 (H-6), 47.1 (H-2), 72.3 (H-4), 76.5 (H-3), 78.1 (H-5), 101.1 (acetal), 126.6 (Ph), 128.7 (Ph), 129.5 (Ph), 137.8 (Ph), 201.6 (H-1). − IR (neat): ṽ = 3437 (broad), 3036, 2975, 2875, 1722, 1453, 1375, 1097, 1057, 1027, 759, 699 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 235 (2) [M$^+$ − 1], 174 (2), 164 (3), 163 (2), 123 (2), 108 (8), 107 (100), 106 (21), 105 (44), 86 (41), 79 (48), 78 (10), 77 (58).

(−)-3,5-*O*-Benzylidene-2,6-*O*-dideoxy-D-*xylo*-hexofuranose (22): Preparation from **19** (94 mg, 0.40 mmol) as described in the general procedure VII. Recrystallization of the crude product from Et_2O and *n*-pentane provided 82 mg pure **22** in four crops. The residue was purified by flash chromatography (SiO_2, Et_2O/cyclohexane, 1:1), which provided another 10 mg of **22** (98% total yield). $[\alpha]_D^{20}$ = −24 (*c* = 0.8, $CHCl_3$). − **The α-Anomer (Crystalline):** M.p. 100−110 °C− ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (d, *J* = 6.7 Hz, 3 H, H-6), 2.07 (dt, *J* = 14.5, 4.7 Hz, 1 H, H-2), 2.49 (dd, *J* = 14.6, 5.7 Hz, 1 H, H-2), 3.93 (t, *J* = 2.2 Hz, 1 H, H-4), 4.18 (qd, *J* = 6.6, 2.0 Hz, 1 H, H-5), 4.51 (dd, *J* = 4.9, 2.2 Hz, 1 H, H-3), 5.49 (s, 1 H, acetal), 5.86 (t, *J* = 5.1 Hz, 1 H, H-1), 7.31−7.39 (m, 3 H, Ph), 7.46−7.52 (m, 2 H, Ph). − NOE experiments: irr. at H-1 → NOE at H-2$_\beta$; irr. at H-3 → NOE at acetal-H, H-4 and H-2$_\alpha$; irr. at H-2$_\beta$ → NOE at H-2$_\alpha$ and H-1; irr. at H-2$_\alpha$ → NOE at H-2$_\beta$ and H-3. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 17.5 (C-6), 41.7 (C-2), 72.7, 75.4, 77.3, 98.6, 100.0, 126.2 (Ph), 128.2 (Ph), 128.8 (Ph), 138.0 (Ph). − IR (KBr): ṽ = 3408 (broad, shoulder at 3288), 2985, 2947, 2931, 1452, 1400, 1345, 1140, 1088, 1031, 1017, 616, 745, 696 cm^{-1}. − MS: *m*/*z* (% rel.int.) = 225 (1) [M$^+$ − 1], 163 (3), 123 (1), 113 (1), 112 (4), 107 (30), 106 (72), 105 (89), 97 (10), 94 (17), 86 (14), 79 (14), 78 (19), 77 (100). − **The β-Anomer (Major Anomer at Equilibrium in $CDCl_3$):** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, *J* = 6.6 Hz, 3 H, H-6), 2.19 (ddd, *J* = 14.0, 5.0, 3.6 Hz, 1 H, H-2), 2.27 (d, *J* = 13.9 Hz, 1 H, H-2), 3.70 (t, *J* = 2.2 Hz, 1 H, H-4), 4.18 (qd, *J* = 6.5, 1.3 Hz, 1 H, H-5), 4.45 (m, 1 H, H-3), 5.43−5.49 (m, 1 H, H-1), 5.52 (s, 1 H, acetal), 7.31−7.41 (m, 3 H, Ph), 7.46−7.52 (m, 2 H, Ph). − NOE experiments: irr. at acetal → NOE at H-3 and H-5; irr. at H-3 → NOE at acetal-H, H-4, and H-2$_\alpha$; irr. at H-4 → NOE at H-3 and H-5; irr. at Me → NOE at H-5. − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 17.3 (C-6), 41.2 (C-2), 73.3, 76.4, 77.4, 99.3, 99.5, 126.0 (Ph), 128.5 (Ph), 129.2 (Ph), 137.7 (Ph).

General Procedure VIII. − Hydrolysis of the Acetal: A solution of the substrate (0.3 mmol) in THF (1.0 mL) was added 0.01 M aqueous trifluoroacetic acid (TFA) (3.0 mL), and the reaction mixture was stirred at room temperature. The reactions were monitored by TLC. After typically 5 h, the reaction mixture was concentrated under reduced pressure. The crude product was dissolved in water (3.0 mL), and the solution was again concentrated. This was repeated, if necessary, until no more TFA or benzaldehyde was detected in the product. NMR spectra were obtained without internal or external standard, and selected peaks in the spectra were calibrated from the literature value.

2-Deoxy-D-*threo*-pentopyranose (2-Deoxy-D-xylose) (27): Preparation from **26** according to general procedure VIII. ^{1}H and ^{13}C NMR spectra were in agreement with previously reported spectra.[17]

2,6-Dideoxy-D-*lyxo*-hexopyranose (D-Oliose) (14): Preparation from **13** according to general procedure VIII. ^{1}H and ^{13}C NMR spectra of the crude product were in agreement with previously reported spectra, and showed a 1:1 composition of the α- and β-pyranose.[8a]

2,6-Dideoxy-D-*arabino*-hexopyranose (D-Olivose) (16): Preparation from **14** according to general procedure VIII. ^{1}H and ^{13}C NMR spectra of the crude product were in agreement with previously reported spectra, and showed an approximately 1:1 composition of the α- and β-pyranose.[8a]

2,6-Dideoxy-DL-*ribo*-hexose (DL-Digitoxose) (19): Preparation from **18** according to general procedure VIII. ^{1}H and ^{13}C NMR spectra of the crude product were in agreement with previously reported spectra.[8a]

2,6-Dideoxy-D-*xylo*-hexose (D-Boivinose) (23), was prepared from **22** according to general procedure VIII. ^{1}H and ^{13}C NMR spectra of the crude product were in agreement with previously reported spectra.[8]

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