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Article

Carbene-Mediated Quaternarization of the Anomeric Position of Carbohydrates: Synthesis of Allylic Ketopyranosides, Access to the Missing #-Gluco and #-Manno Stereoisomers, and Preparation of Quaternary 2-Deoxy-2-Acetamido Sugars

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Carbene-Mediated Quaternarization of the Anomeric Position of Carbohydrates: Synthesis of Allylic Ketopyranosides, Access to the Missing *α-Gluco* and *β-Manno* Stereoisomers, and Preparation of Quaternary 2-Deoxy-2-Acetamido Sugars

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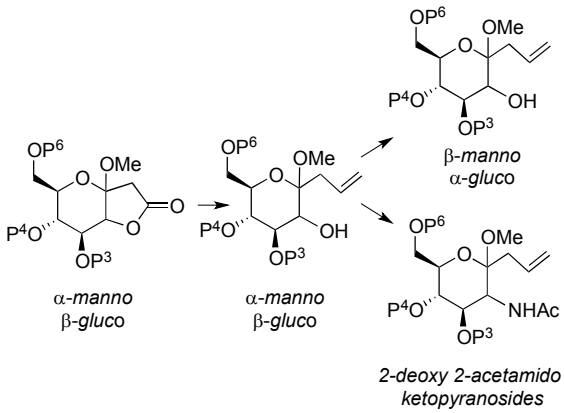
Graphical Abstract:



Abstract:

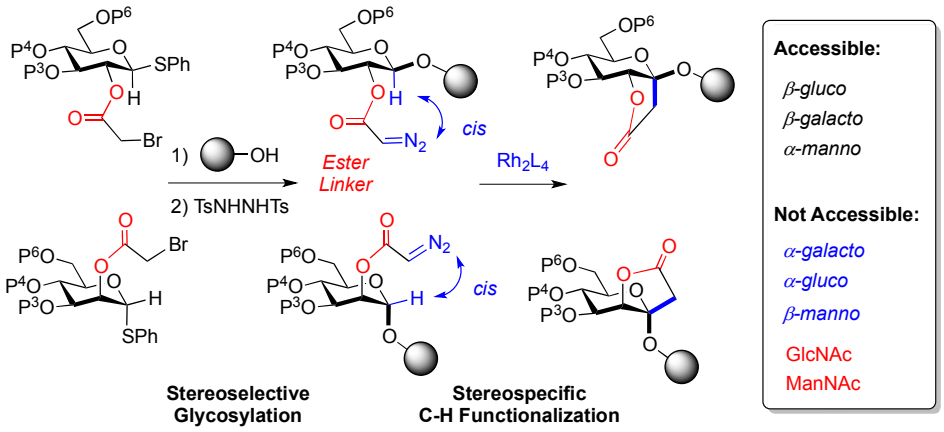
Following our work on the C-H functionalization of carbohydrates by 1,5 insertion of metal-carbenes, we report herein the robust and scalable conversion of sugar γ-lactones into highly valuable glycosides having a quaternary anomeric position substituted by an

allyl chain ready for further functionalization. A divergent synthetic approach furthermore provided a straightforward access to ketopyranosides with a large chemo- and stereodiversity at position 2.

Introduction:

The field of glycobiology has made significant progress in recent years, in particular as a result of the emergence of new synthetic tools in carbohydrate chemistry. Efficient and innovative synthetic methods have contributed to a better understanding of the role played by complex oligosaccharides in numerous biological events, and paved the way to the new era of chemical glycobiology.[1] In this context, we recently reported a new approach toward ketopyranosides, in which quaternarization of the anomeric position was performed in a late stage of the synthetic process.[2] After glycosylation with anchimeric assistance of a 2-*O*-bromoacetyl, functionalization of the anomeric C-H bond with retention of configuration was promoted by 1,5 insertion of a Rh(II)-carbene.[3] Apart from allowing a more efficient access to ketopyranosides having an axial aglycone, this strategy also opened the way to the unprecedented β-anomers (Scheme 1). Although critical to ensure a clean C-H functionalization process, anchoring the metal-carbene at position 2 also had some limitations. First, only ketopyranosides in the *α-manno, β-gluco* and *β-galacto* series could be obtained because insertion into the anomeric C-H bond took place after formation of a *1,2-trans* glycosidic linkage. Moreover, 2-deoxy-2-amino sugars with a quaternary anomeric position, which are highly desirable since GlcNAc, GalNAc and ManNAc are major components of glycoconjugates,[4,5] could not be prepared by direct functionalization of the anomeric C-H bond of 2-deoxy 2-amino sugars. In fact, only complex mixtures were obtained, if an

amide tether between the metal-carbene and the sugar moiety replaced the ester linkage.[6]



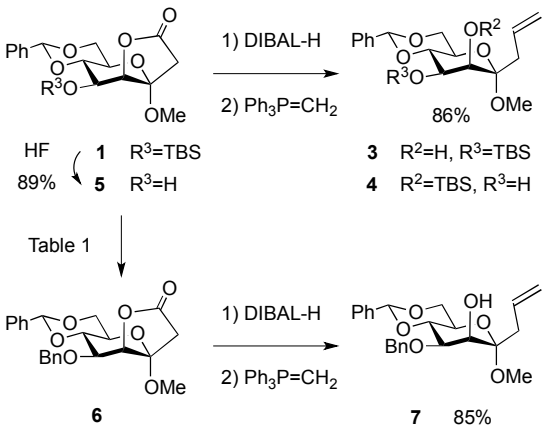
Scheme 1. Carbene-Mediated Quaternarization of the Anomeric Position: Scope and Limitations

The design of new chemical tools for glycobiology with a ketopyranosidic central core would require a straightforward and robust access toward compounds covering a larger chemical space than the *α-manno*, *β-gluco* and *β-galacto* series. In this context, we would like to report herein transformation of *α-manno* and *β-gluco* γ-lactones into ketopyranosides bearing an allyl pending chain, and the efficient chemical and stereochemical diversification at position 2 following a diversity-oriented approach.

Results and Discussion:

Sugar lactones **1** (Scheme 2) and **2** (Scheme 3) with a *tert*-butyldimethylsilyl ether protecting group at position 3 were routinely prepared on gram scale by decomposition of diazo sugars under $Rh_2(OAc)_4$ catalysis in refluxing 1,2 dichloroethane.[7] Since partial

reduction of **1** with DIBAL-H in DCM at -78 °C and Wittig olefination gave a mixture of *C,O*-glycosides **3** and **4** by migration of the *tert*-butyldimethylsilyl group (Scheme 2), switching toward a robust benzyl ether was thus considered. Although deprotection of lactone **1** with TBAF resulted in massive degradation, HF/Pyridine gave alcohol **5** in 89% yield after purification by silica gel flash chromatography.

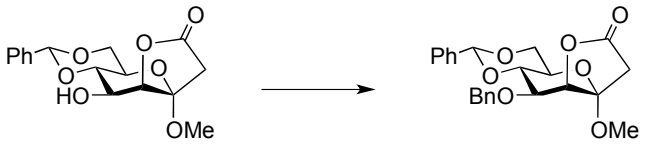


Scheme 2. Preparation of ketopyranoside **7** in the *α-manno* series.

Not surprisingly, benzylation under Williamson's conditions induced degradation of lactone **5**.[8] Benzyl 2,2,2-trichloroacetimidate (BnTCA)[9] gave **6** in moderate yield and low purity because Lewis or Brønsted acid activation induced competitive cleavage of the 4,6-*O*-benzylidene function (Table 1, entries 1-3). Benzylation of **5** was next attempted with 2-benzyloxy-1-methylpyridinium triflate (BnPYR) and MgO.[10] Even if conversion remained partial, pure lactone **6** was obtained in 66% yield after prolonged heating in trifluorotoluene (entries 4 and 5). Under microwave irradiation,[11] the reaction time was reduced to 9 h, and the yield improved to 74%, without affecting the purity of **6** (entry 6). Finally, clean and full conversion of **5** was achieved with benzyl bromide (BnBr) and silver(I) oxide (Ag_2O) in refluxing dichloromethane to give pure 3-*O*-benzyl lactone **6** in

88% isolated yield after silica gel flash chromatography (entries 7 and 8).[12] Partial reduction of **6** with DIBAL-H at -78 °C in DCM and Wittig olefination gave α-ketopyranoside **7** having a complete set of orthogonal protecting groups in 85% yield over two steps (Scheme 2).

Table 1. Benzylation at position 3 in the *α-manno* series.



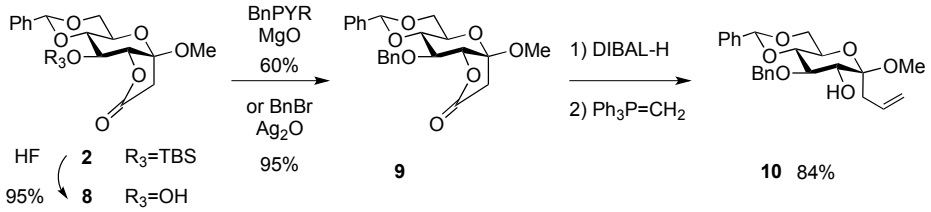
5 **6**

Entry	Reagent (equiv.)	Additive (equiv.)	Temp. (°C)	Time (h.)	Conv. (%)[a]	Yield (%)[b]
1[c]	BnTCA (3)	TfOH (0.2)	0	1	70	57
2[c]	BnTCA (3)	TMSOTf (0.2)	0	1.5	100	31
3[c]	BnTCA (3)	$BF_3.OEt_2$ (0.2)	0	1.5	50	12
4[d]	BnPYR (2)	MgO (2)	85	48	74	66
5[d]	BnPYR (2)	MgO (2)	100	48	80	64
6[d,e]	BnPYR (2)	MgO (2)	80	10	80	74
7[c]	BnBr (1.2)	Ag_2O (1.2)	R.T.	4	0	-
8[c]	BnBr (3)	Ag_2O (2.4)	40	4	100	88

[a]: evaluated by ^1H NMR analysis of the crude; [b]: isolated after flash chromatography

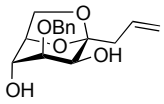
[c]: CH_2Cl_2 as solvent; [d]: trifluorotoluene as solvent; [e]: microwave irradiation.

The same sequence was next performed in the *β-gluco* series. Desilylation of **2** with HF/pyridine followed by benzylation either with BnPYR/MgO or BnBr/Ag_2O gave lactone **9** with a 3-*O*-benzyl ether in 57 and 90% yield respectively over two steps. After partial reduction with DIBAL-H and olefination, β-ketopyranoside **10** was finally obtained in 84% yield (Scheme 3).



Scheme 3. Preparation of ketopyranoside **10** in the *β-gluco* series.

Having developed a robust and scalable access to *α-manno* and *β-gluco C,O*-glycosides **7** and **10**, ketopyranosides **15** and **16** in the *α-gluco* and *β-manno* series, as well as 2-deoxy 2-acetamido sugars with a quaternary anomeric position **17**-**20**, were next prepared following a diversity-oriented approach (scheme 4). To our surprise, oxidation of **7** under Swern conditions gave a complex mixture from which 1,6-anhydro derivative **13**, resulting from cleavage of the glycosidic bond, was identified. Methyl 2-ulosides **11** and **12** were finally prepared in 64 and 65% yield respectively by oxidation of **7** and **10** with Dess-Martin Periodinane (DMP). It is worth of note that pyridine should be used as a cosolvant,[13] and the amount of DMP carefully controlled, in order to prevent formation of **14**, presumably obtained by radical hydrogen abstraction at position 3 followed by β-fragmentation of the benzyl ether.



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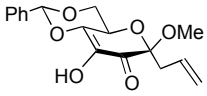
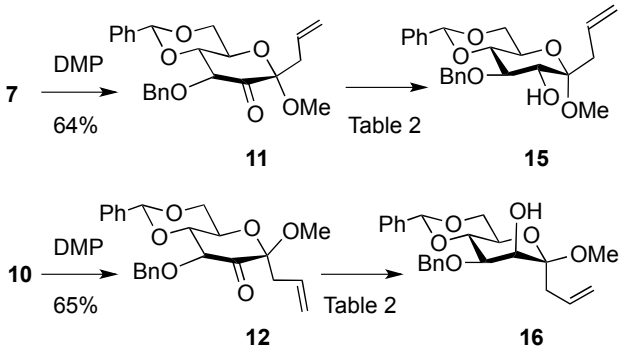


14

Reduction of **11** and **12** into the missing *α-gluco* and *β-manno* ketopyranosides **15** and **16** was next investigated with $NaBH_4$, DIBAL-H and L-Selectride.[14]



Scheme 4. Preparation and reduction of methyl 2-ulosides **11** and **12**.

From methyl α-uloside **11**, ketopyranoside **15** in the *α-gluco* series was obtained as the major diastereoisomer with $NaBH_4$ or DIBAL-H, (table 2, entries 1 and 2), whereas L-Selectride mainly gave back the quaternary mannoside **7**. Similarly to previous reports from the literature,[15] reduction of **11** by $NaBH_4$ mainly occurred by axial attack of the hydride, thus showing that the quaternary anomeric centre had little influence on the stereochemical outcome of the reaction. However, reduction of uloside **12** with $NaBH_4$ did not yield β–mannoside **16** as expected,[16] but rather a 1:1 mixture of epimers. The quaternary anomeric centre, in addition to the cyclic 4,6-*O*-benzylidene,[17] thus had a dramatic impact on the stereochemical outcome of the reduction in the *β* series. The desired methyl β-ketopyranoside **16** in the *manno* series was finally obtained with complete stereocontrol by reduction with L-selectride.[18]

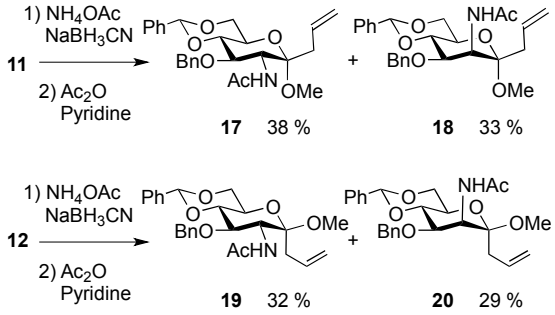
Table 2. Reduction of ulosides **11** and **12**.

Entry	2-uloside	Reagent	Alcohols (d.r.)[a]	Yield (%)[b]
1	**11**	$NaBH_4$	**7/15** (3:7)	91
2	**11**	DIBAL-H	**7/15** (1:3)	51
3	**11**	L-Selectride	**7/15** (4:1)	56
4	**12**	$NaBH_4$	**10/16** (1:1)	60
5	**12**	DIBAL-H	**10/16** (7:1)	51
6	**12**	L-Selectride	**10/16** (0:1)	61

[a]: evaluated by ^1H NMR analysis of the crude; [b]: isolated after flash chromatography.

With suitable conditions for accessing the missing *α-gluco* and *β-manno* series in hands, we next turned our attention toward the preparation of quaternary 2-deoxy 2-acetamido sugars from methyl 2-ulosides **11** and **12** (scheme 5). Since classical approaches relying on substitution of 2-*O*-sulfonates with azides,[19] or on formation of oximes followed by reductive cleavage of the N-O bond,[20] all failed despite extensive

efforts, direct reductive amination of **11** and **12** with NH_4OAc and $NaBH_3CN$ was thus considered.[21] Under microwave irradiation,[22] amination was performed at 80 °C without degradation of the starting materials, but competitive reduction of **11** and **12** into alcohols **7**/**15** and **10**/**16** gave a complex mixture. By delaying introduction of the reducing agent after 10 min heating with NH_4OAc alone, the desired 2-deoxy 2-acetamido sugars **17**-**20** were finally obtained in good yield after acetylation. Configuration of **17**-**20** was determined on the basis of vicinal coupling constants between H_2 and H_3 (J = 4.5 Hz for **18** in the *manno* series, and J = 9.2 Hz for **19** with a *gluco* configuration).



Scheme 5. Preparation of 2-deoxy 2-acetamido ketopyranosides **17**-**20**.

Overall, we reported herein the preparation of eight non-natural sugars derivatives with a quaternary anomeric position substituted by an allyl pending chain. From lactones **1** and **2**, a robust and scalable synthetic sequence first gave α-*manno* and β-*gluco* ketopyranosides **7** and **10** in 67 and 76% yield respectively over 4 steps. After oxidation into key ulosides **11** and **12**, a diversity-oriented approach provided a straightforward access to ketopyranosides **15** and **16** in the missing α-*gluco* and β-*manno* series, as well as to the four stereoisomers **17**-**20** of unprecedented quaternary 2-deoxy 2-acetamido sugars. Having in hands a large diversity of non-natural carbohydrate derivatives having a quaternary anomeric position substituted by an allyl chain ready for further

functionalization, new chemical tools for glycobiology are currently under preparation in our laboratory.

Experimental Section

General Information and Method. For reactions, solvents were purchased anhydrous (dichloromethane, and pyridine) or distilled (tetrahydrofuran over sodium/benzophenone). All reactions were conducted under an argon atmosphere. All reagents were used as received unless otherwise indicated. Reactions were monitored by thin-layer chromatography with silica gel 60 F254 pre-coated aluminium plate (0.25 mm). Visualization was performed under UV light and phosphomolybdic acid oxidation. ^{1}H NMR spectra were recorded at 300 MHz, and ^{13}C NMR spectra at 75 MHz. Abbreviations used for peak multiplicities are s: singlet, d: doublet, t: triplet, q: quadruplet and m: multiplet. Coupling constants *J* are in Hz and chemical shifts are given in ppm and calibrated with $CDCl_3$ (residual solvent signals). Carbon multiplicities were assigned by distortionless enhancement by polarization transfer (DEPT) experiments. The ^{1}H and ^{13}C signals were assigned by COSY and HSQC experiments. Accurate mass measurements (HRMS) were performed with a Q-TOF analyser. Infrared spectra (IR) were recorded by application on a Single Reflection Attenuated Total Reflectance (ATR) Accessories, and data are reported in cm^{-1}. Optical rotations were determined with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g per 100 mL. Melting points are uncorrected. Microwave experiments were conducted in a Biotage Initiator equipped with a monomode cavity with a microwave power delivery system ranging from 0 to 850 W allowing pressurized reactions (0 to 30 bars) to be carried out in sealed glass vials (0.5 to 20 mL) equipped

with a snap cap and a silicon septum. The temperature (0 to 300 °C) was monitored via a contact-less infrared sensor and was calibrated with a Ruby Thermometer.

(2*R*,4*aR*,5*aS*,8*aS*,9*S*,9*aS*)-9-hydroxy-5a-methoxy-2-phenylhexahydrofuro[2',3':5,6]pyrano[3,2-*d*][1,3]dioxin-7(8aH)-one 5. To a solution of lactone **1** (1.456 g, 3.334 mmol) in THF (50 mL), was added a solution of HF.pyridine (dry THF/dry pyridine/HF.pyridine, 2:2:1, 65.5 mL, 333 mmol) at room temperature. After 18 h, ethyl acetate (150 mL) and a saturated solution of $NaHCO_3$ (600 mL) were carefully added. After 30 min, the organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 150 mL). The combined organic layers were dried ($MgSO_4$), filtrated, and concentrated under reduce pressure. Purification by silica gel chromatography (cyclohexane/ethyl acetate 1.5:1) gave **5** as a white foam (946 mg, 89%):

R_f = 0.22 (Silica, cyclohexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.57-7.26 (m, 5H, H_{Ar}), 5.56 (s, 1H, H7), 4.61 (d, *J* = 4.2 Hz, 1H, H2), 4.28-4.24 (m, 1H, H6), 4.09 (dd, *J* = 9.3, 4.2 Hz, 1H, H3), 3.86-3.70 (m, 3H, H4, H5, H6), 3.37 (s, 3H, OMe), 2.82 (d, *J* = 16.3 Hz, 1H, $\underline{CH_2}$-C=O), 2.61 (d, *J* = 16.3 Hz, 1H, $\underline{CH_2}$-C=O), 2.50 (br s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 171.4 (C=0), 136.9 (Cq_{Ar}), 129.4 (C_{Ar}), 128.4 (C_{Ar}), 126.3 (C_{Ar}), 103.5 (C1), 102.1 (C7), 81.0 (C2), 77.6 (C4), 68.1 (C6), 67.7 (C3), 64.3 (C5), 51.9 (OMe), 40.4 ($\underline{CH_2}$-C=O); FT-IR (film): 3467, 2922, 2859, 1778, 1455, 1393, 1300, 1254, 1226, 1165, 1191, 1088, 1025, 999, 954, 917, 774, 702, 670, 568, 535 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{16}H_{22}NO_7$ $[M + NH_4]^+$ 340.1396, found 340.1395; $[\alpha]_D^{20}$ = - 58 ($CHCl_3$, c = 1.85).

(2*R*,4*aR*,5*aR*,8*aR*,9*S*,9*aS*)-9-hydroxy-5a-methoxy-2-phenylhexahydrofuro[2',3':5,6]pyrano[3,2-*d*][1,3]dioxin-7(8aH)-one 8. To a

solution of lactone **2** (800 mg, 1.83 mmol) in THF (30 mL), was added a solution of HF.pyridine (dry THF/dry pyridine/HF.pyridine, 2:2:1, 21 mL, 183 mmol) at room temperature. After 18 h, ethyl acetate (100 mL) and a saturated solution of $NaHCO_3$ (400 mL) were carefully added. After 30 min, the organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 150 mL). The combined organic layers were dried ($MgSO_4$), filtrated, and concentrated under reduce pressure. Purification by silica gel chromatography (cyclohexane / ethyl acetate 1.5:1) gave **8** as a white foam (560 mg, 95%). R_f = 0.38 (Silica, dichloromethane/ethyl acetate 15:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.50-7.38 (m, 5H, H_{Ar}), 5.57 (s, 1H, H7), 4.43 (d, *J* = 6.4 Hz, 1H, H2), 4.35 (dd, *J* = 10.0, 4.9 Hz, 1H, H6), 3.91 (dd, *J* = 10.2, 6.4 Hz, 1H, H3), 3.78-3.73 (m, 2H, H6, H4), 3.62 (ddd, *J* = 10.0, 9.1, 4.9 Hz, 1H, H5), 3.38 (s, 3H, OMe), 2.93 (br s, 1H, OH), 2.82 (d, *J* = 17.1 Hz, 1H, $\underline{CH_2}$-C=O), 2.67 (d, *J* = 17.1 Hz, 1H, $\underline{CH_2}$-C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 172.0 (C=O), 136.7 (Cq_{Ar}), 129.6 (C_{Ar}), 128.6 (C_{Ar}), 126.4 (C_{Ar}), 103.8 (C1), 102.0 (C7), 83.4 (C2), 78.1 (C4), 72.8 (C3), 68.7 (C6), 66.0 (C5), 50.4 (OMe), 35.9 ($\underline{CH_2}$-C=O); FT-IR (film): 3454, 2922, 2857, 1788, 1456, 1380, 1212, 1167, 1079, 1007, 918, 835, 754, 699, 542 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{16}H_{22}NO_7$ $[M + NH_4]^+$ 340.1396, found 340.1396; $[\alpha]_D^{20}$ = + 3 ($CHCl_3$, c = 1.0).

(2*R*,4*aR*,5*aS*,8*aS*,9*S*,9*aR*)-9-(benzyloxy)-5a-methoxy-2-phenylhexahydrofuro[2',3':5,6]pyrano[3,2-*d*][1,3]dioxin-7(8aH)-one 6. Procedure A: A suspension of alcohol **5** (100 mg, 0.310 mmol), MgO (25 mg, 0.620 mmol) and 2-benzyloxy-methylpyridinium triflate (217 mg, 0.620 mmol) in trifluorotoluene (0.6 mL) under an argon atmosphere was heated under microwave irradiation at 85 °C. After 10 h, dichloromethane (3 mL) and a saturated solution of $NaHCO_3$ (3 mL) were added, and the mixture was stirred until it became homogenous. After separation, the aqueous layer was extracted with dichloromethane, the combined organic phases were dried ($MgSO_4$),

filtered, and concentrated under reduce pressure. After purification by silica gel chromatography (cyclohexane/ethyl acetate 3:1), **6** was obtained as a colourless oil (85 mg, 66%). Procedure B: A suspension of **5** (300 mg, 0.93 mmol), Ag_2O (646.5 mg, 2.79 mmol) and benzyl bromide (265 μL, 2.23 mmol) in dichloromethane (2.1 mL) under an argon atmosphere was heated at 40 °C in a sealed tube (dark). After 4h30, the reaction mixture was diluted with dichloromethane (20 mL), filtered through a Celite pad, and added with a saturated solution of $NaHCO_3$ (20 mL). After separation of the organic layer, the aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. After purification by silica gel chromatography (cyclohexane/ethyl acetate 2:1) **6** was obtained as a colourless oil (340 mg, 88%).

R_f = 0.28 (Silica, cyclohexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.53-7.25 (m, 10H, H_{Ar}), 5.61 (s, 1H, H7), 4.88 (d, *J* = 12.3 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.78 (d, *J* = 12.3 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.58 (d, *J* = 3.6 Hz, 1H, H2), 4.28 (dd, *J* = 9.8, 3.6 Hz, 1H, H6), 4.06 (t, *J* = 9.5 Hz, 1H, H4), 3.99 (dd, *J* = 9.5, 3.6 Hz, 1H, H3), 3.77 (t, *J* = 9.8 Hz, 1H, H6), 3.76-3.74 (m, 1H, H5), 3.30 (s, 3H, OMe), 2.80 (d, *J* = 16.5 Hz, 1H, $\underline{CH_2}$-C=O), 2.66 (d, *J* = 16.5 Hz, 1H, $\underline{CH_2}$-C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 171.6 (C=O), 137.8 (Cq_{Ar}), 137.2 (Cq_{Ar}), 129.2 (C_{Ar}), 128.5 (C_{Ar}), 128.4 (C_{Ar}), 127.9 (C_{Ar}), 126.1 (C_{Ar}), 103.7 (C1), 101.6 (C7), 80.1 (C2), 77.6 (C4), 73.2 (C3), 73.1 (O-$\underline{CH_2}$-Ph), 68.3 (C6), 64.6 (C5), 51.9 (OMe), 40.3 ($\underline{CH_2}$-C=O); FT-IR (film): 2933, 2871, 1797, 1493, 1454, 1377, 1302, 1282, 1217, 1177, 1155, 1096, 1077, 1004, 962, 750, 698 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{23}H_{25}O_7$ $[M + H]^+$ 413.1600, found 413.1613; $[\alpha]_D^{20}$ = - 40 ($CHCl_3$, c = 1.0).

(2*R*,4*aR*,5*aR*,8*aR*,9*S*,9*aR*)-9-(benzyloxy)-5a-methoxy-2-phenylhexahydrofuro[2',3':5,6]pyrano[3,2-*d*][1,3]dioxin-7(8aH)-one 9. Procedure

A: A suspension of alcohol **8** (100 mg, 0.310 mmol), MgO (25 mg, 0.620 mmol) and 2-benzyloxy-methylpyridinium triflate (217 mg, 0.620 mmol) in trifluorotoluene (0.6 mL) under an argon atmosphere was heated under microwave irradiation at 85 °C. After 10 h, dichloromethane (3 mL) and a saturated solution of $NaHCO_3$ (3 mL) were added, and the mixture was stirred until it became homogenous. After separation, the aqueous layer was extracted with dichloromethane, the combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduce pressure. After purification by silica gel chromatography (cyclohexane/ethyl acetate 3:1), **9** was obtained as a colourless oil (77 mg, 60%). Procedure B: A suspension of **8** (300 mg, 0.93 mmol), Ag_2O (646.5 mg, 2.79 mmol) and benzyl bromide (265 μL, 2.23 mmol) in dichloromethane (2.1 mL) under an argon atmosphere was heated at 40 °C in a sealed tube (dark). After 3h30, the reaction mixture was diluted with dichloromethane (20 mL), filtered through a Celite pad, and added with a saturated solution of $NaHCO_3$ (20 mL). After separation, the aqueous layer was extracted with dichloromethane (2 x 20 mL), and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. After purification by silica gel chromatography (cyclohexane/ethyl acetate 2:1) **9** was obtained as a colourless oil (365 mg, 95%). R_f = 0.34 (Silica, cyclohexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.52-7.31 (m, 10H, H_{Ar}), 5.63 (s, 1H, H7), 4.85 (s, 2H, O-$\underline{CH_2}$-Ph), 4.54 (d, *J* = 5.6 Hz, 1H, H2), 4.34 (dd, *J* = 10.3, 4.8 Hz, 1H, H6), 3.99 (t, *J* = 9.7 Hz, 1H, H4), 3.87-3.74 (m, 2H, H3, H6), 3.67 (dt, *J* = 9.7, 4.8 Hz, 1H, H5), 3.40 (s, 3H, OMe), 2.86 (d, *J* = 17.2 Hz, 1H, $\underline{CH_2}$-C=O), 2.69 (d, *J* = 17.2 Hz, 1H, $\underline{CH_2}$-C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 171.6 (C=O), 137.4 (Cq_{Ar}), 136.9 (Cq_{Ar}), 129.2 (C_{Ar}), 128.5 (C_{Ar}), 128.4 (C_{Ar}), 128.0 (C_{Ar}), 126.1 (C_{Ar}), 103.9 (C1), 101.6 (C7), 83.9 (C2), 78.8 (C3), 78.2 (C4), 73.7 (O-$\underline{CH_2}$-Ph), 68.9 (C6), 66.4 (C5), 50.7 (OMe), 36.8 ($\underline{CH_2}$-C=O); FT-IR (film): 2933, 1793, 1605, 1497, 1454, 1372, 1331, 1268, 1245, 1213, 1170, 1091, 1028, 916, 890, 752, 698,

601 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{23}H_{24}O_7Na$ $[M + Na]^+$ 435.1420, found 435.1415; $[\alpha]_D^{20}$ = + 5 ($CHCl_3$, c = 1.0).

(2*R*,4*aR*,6*S*,7*S*,8*R*,8*aR*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-ol 7. To a solution of **6** (520 mg, 1.26 mmol) in CH_2Cl_2 (10 mL) at -78 °C was added drop-wise a 1 M solution of DIBAL-H in hexanes (1.388 mL, 1.388 mmol). After 15 min at -78 °C, the mixture was quenched with methanol, and added with CH_2Cl_2 (20 mL) and Rochelle salts (1 M, 20 mL). After 12 h of vigorous stirring at room temperature, the organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. Filtration over a silica plug delivered the lactol as a mixture of diastereoisomers. A suspension of methyltriphenylphosphonium bromide (678 mg, 1.89 mmol) in THF (8 mL) at 0 °C was added with potassium *tert*-butoxide (213 mg, 1.89 mmol) and a solution of lactol in THF (2 mL). After 15 min stirring at room temperature, CH_2Cl_2 (25 mL) and water (15 mL) were added. After separation, the aqueous layer was extracted with dichloromethane (3 x 25 mL), and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. Purification by silica gel chromatography (dichloromethane/ethyl acetate from 100:0 to 90:10) gave **7** as a colorless oil (442 mg, 85% over 2 steps). R_f = 0.53 (silica, cyclohexane / ethyl acetate 2.5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.54-7.29 (m, 10H, H_{Ar}), 5.77 (dddd, *J* = 17.1, 10.3, 7.3, 6.7 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.63 (s, 1H, H7), 5.28-5.18 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.86 (d, *J* = 11.9 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.74 (d, *J* = 11.9 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.30 (dd, *J* = 10.4, 4.8 Hz, 1H, H6), 4.11 (t, *J* = 9.1 Hz, 1H, H4), 4.04-3.99 (m, 2H, H2, H3), 3.88 (t, *J* = 10.4 Hz, 1H, H6), 3.70 (ddd, *J* = 10.4, 9.1, 4.8 Hz, 1H, H5), 3.27 (s, 3H, OMe), 2.73 (m, 2H, $\underline{CH_2}$-CH=CH_2, OH), 2.54 (dd, *J* = 14.7, 6.7 Hz, 1H, $\underline{CH_2}$-CH=CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 138.1 (Cq_{Ar}), 137.6

(Cq_{Ar}), 131.6 (CH_2-<u>CH</u>=CH_2), 128.9 (C_{Ar}), 128.5 (C_{Ar}) , 128.2 (C_{Ar}), 127.85 (C_{Ar}), 127.83 (C_{Ar}), 126.1 (C_{Ar}), 119.1 (CH_2-CH=<u>CH_2</u>), 102.6 (C1), 101.5 (C7), 78.6 (C4), 76.1 (C3), 72.8 (O-<u>CH_2</u>-Ph), 69.5 (C2), 68.9 (C6), 64.1 (C5), 47.4 (OMe), 35.2 (<u>CH_2</u>-CH=CH_2); FT-IR (film): 3482, 3033, 2912, 1643, 1497, 1454, 1374, 1211, 1094, 1059, 1026, 1004, 915, 848, 817, 745, 695, 649 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{29}O_6$ $[M + H]^+$ 413.1964, found 413.1963; $[\alpha]_D^{20}$ = - 26 ($CHCl_3$, c = 1.0).

(2*R*,4*aR*,6*R*,7*R*,8*R*,8*aR*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-ol 10. To a solution of **9** (450 mg, 1.08 mmol) in CH_2Cl_2 (3 mL) at -78 °C was added drop wise a 1 M solution of DIBAL-H in hexanes (1.42 mL, 1.42 mmol). After 15 min at -78 °C, the mixture was quenched with methanol, and added with CH_2Cl_2 (5 mL) and Rochelle salts (1 M, 5 mL). After 12 h of vigorous stirring at room temperature, the organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. Filtration over a silica plug delivered the lactol as a mixture of diastereoisomers. A suspension of methyltriphenylphosphonium bromide (1.02 g, 2.86 mmol) in THF (2.5 mL) at 0 °C was added with potassium *tert*-butoxide (321 mg, 2.86 mmol) and a solution of lactol in THF (2.5 mL). After 15 min stirring at room temperature, CH_2Cl_2 (10 mL) and water (10 mL) were added. After separation, the aqueous layer was extracted with dichloromethane (3 x 15 mL), and the combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. Purification by silica gel chromatography (cyclohexane/ethyl acetate from 3:1) gave **10** as a colorless oil (374 mg, 84% over 2 steps). R_f = 0.28 (silica, cyclohexane/ethyl acetate 3:1); ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.51-7.29 (m, 10H, H_{Ar}), 5.91 (dddd, *J* = 18.0, 11.8, 7.8, 6.3 Hz, 1H, CH_2-<u>CH</u>=CH_2), 5.59 (s, 1H, H7), 5.19-5.14 (m, 2H, CH_2-CH=<u>CH_2</u>), 5.02 (d, *J* = 11.4 Hz, 1H, O-<u>CH_2</u>-Ph), 4.76

(d, *J* = 11.4 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.31 (dd, *J* = 10.4, 4.5 Hz, 1H, H6), 3.93-3.90 (m, 1H, H3), 3.80-3.72 (m, 3H, H2, H4, H6), 3.60 (td, *J* = 9.4, 4.5 Hz, 1H, H5), 3.37 (s, 3H, OMe), 2.72 (dd, *J* = 15.2, 6.3 Hz, 1H, $\underline{CH_2}$-CH=CH_2), 2.59 (dd, *J* = 15.2, 7.8, Hz, 1H, $\underline{CH_2}$-CH=CH_2), 2.37 (d, 1H, OH, *J* = 2.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 138.2 (Cq_{Ar}), 137.3 (Cq_{Ar}), 131.6 (CH_2-$\underline{CH}$=CH_2), 129.0 (C_{Ar}), 128.5 (C_{Ar}), 128.3 (C_{Ar}), 128.1 (C_{Ar}), 127.9 (C_{Ar}), 125.9 (C_{Ar}), 118.2 (CH_2-CH=$\underline{CH_2}$), 102.4 (C1), 101.2 (C7), 82.2 (C2), 80.1 (C4), 74.6 (O-$\underline{CH_2}$-Ph), 71.6 (C3), 69.2 (C6), 64.7 (C5), 48.9 (OMe), 35.3 ($\underline{CH_2}$-CH=CH_2); FT-IR (film): 3479, 3362, 2922, 2854, 1454, 1375, 1212, 1177, 1076, 1059, 1026, 1006, 962, 915, 865, 762, 745, 697, 660, 488 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{32}NO_6$ $[M + NH_4]^+$ 430.2230, found 430.2228; $[\alpha]_D^{20}$ = + 10 ($CHCl_3$, c = 1.0).

(2*R*,4*aR*,6*S*,8*R*,8*aR*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenyltetrahydropyrano[3,2-*d*][1,3]dioxin-7(6H)-one 11. A solution of Dess-Martin periodinane (144 mg, 0.338 mmol) in pyridine (1 mL) was stirred at room temperature for 30 min, and added with a solution of alcohol **7** (140 mg, 0.338 mmol) in dichloromethane (1 mL). After 10 h at room temperature, additional Dess-Martin periodinane (144 mg, 0.338 mmol) was added to the reaction mixture. After 10 h, TLC revealed complete consumption of the starting material, and dichloromethane (8 mL), a saturated solution of $NaHCO_3$ (4 mL) and a saturated solution of $Na_2S_2O_3$ (4 mL) were added. After 4 h, the organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. After purification by silica gel chromatography (cyclohexane/ethyl acetate 5:1), ketone **11** was obtained as a colorless film (90 mg, 64%). R_f = 0.85 (silica, cyclohexane / ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.53-7.27 (m, 10H, H_{Ar}), 5.81 (dddd, *J* = 17.6, 10.4, 7.4, 6.2 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.56 (s, 1H, H7), 5.21-5.12 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.93 (d, *J* = 12.0 Hz, 1H, O-

$\underline{CH_2}$-Ph), 4.69 (d, *J* = 12.0 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.61 (d, *J* = 10.4 Hz, 1H, H3), 4.39 (dd, *J* = 10.3, 5.3 Hz, 1H, H6), 4.09 (td, *J* = 10.3, 5.3 Hz, 1H, H5), 3.86-3.78 (m, 2H, H4, H6), 3.31 (s, 3H, OMe), 2.70-2.56 (m, 2H, $\underline{CH_2}$-CH=CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 198.2 (C2), 137.7 (Cq_{Ar}), 137.0 (Cq_{Ar}), 131.5 (CH_2-$\underline{CH}$=CH_2), 129.2 (C_{Ar}), 128.4 (C_{Ar}), 128.3 (C_{Ar}), 127.9 (C_{Ar}), 127.8 (C_{Ar}), 126.2 (C_{Ar}), 118.9 (CH_2-CH=$\underline{CH_2}$), 102.2 (C1), 101.1 (C7), 82.4 (C4), 80.5 (C3), 73.4 (O-$\underline{CH_2}$-Ph), 68.8 (C6), 63.9 (C5), 48.6 (OMe), 35.4 ($\underline{CH_2}$-CH=CH_2); FT-IR (film): 3063, 3030, 2924, 2854, 1720, 1602, 1495, 1454, 1361, 1313, 1270, 1207, 1176, 1095, 1069, 1027, 910, 733, 712, 695, 604, 461 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{30}NO_6$ $[M + NH_4]^+$ 428.2073, found 428.2071; $[\alpha]_D^{20}$ = - 7 ($CHCl_3$, c = 2.5).

(2*R*,4*aR*,6*R*,8*R*,8*aR*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenyltetrahydropyrano[3,2-*d*][1,3]dioxin-7(6H)-one 12. A solution of Dess-Martin periodinane (236 mg, 0.557 mmol) in pyridine (2 mL) was stirred at room temperature for 30 min, and added with a solution of alcohol **10** (230 mg, 0.557 mmol) in dichloromethane (2 mL). After 10 h at room temperature, additional Dess-Martin periodinane (236 mg, 0.557 mmol) was added to the reaction mixture. After 10 h, TLC revealed complete consumption of the starting material, and dichloromethane (20 mL), a saturated solution of $NaHCO_3$ (10 mL) and a saturated solution of $Na_2S_2O_3$ (10 mL) were added. After 4 h, the organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 20 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduce pressure. After purification by silica gel chromatography (cyclohexane/ethyl acetate 5:1), ketone **12** was obtained as a colorless film (150 mg, 65%). R_f = 0.82 (silica, cyclohexane / ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.53-7.29 (m, 10H, H_{Ar}), 5.76 (ddt, *J* = 17.3, 10.2, 7.0 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.60 (s, 1H, H7), 5.17-5.02 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.98 (d, *J* = 12.2 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.78 (d, *J* = 12.2 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.43-4.40 (m, 1H, H6), 4.22 (d, *J* = 10.2 Hz,

1H, H3), 3.98-3.76 (m, 3H, H4, H5, H6), 3.33 (s, 3H, OMe), 2.55-2.53 (m, 2H, $\underline{CH_2}$-CH=CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 201.4 (C2), 137.3 (Cq_{Ar}), 136.9 (Cq_{Ar}), 129.8 (CH_2-$\underline{CH}$=CH_2), 129.3 (C_{Ar}), 128.6 (C_{Ar}), 128.4 (C_{Ar}), 128.20 (C_{Ar}), 128.17 (C_{Ar}), 126.2 (C_{Ar}), 119.8 (CH_2-CH=$\underline{CH_2}$), 104.9 (C1), 101.1 (C7), 81.4 (C4), 81.3 (C3), 74.0 (O-$\underline{CH_2}$-Ph), 69.1 (C6), 65.1 (C5), 51.9 (OMe), 38.9 ($\underline{CH_2}$-CH=CH_2); FT-IR (film): 3040, 2921, 2857, 1735, 1640, 1497, 1455, 1441, 1370, 1243, 1214, 1132, 1076, 999, 876, 741, 699, 459 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{30N}O_6$ $[M + NH_4]^+$ 428.2073, found 428.2066; $[\alpha]_D^{20}$ = - 10 ($CHCl_3$, c = 2.1).

(2*R*,4*aR*,6*S*,7*R*,8*R*,8*aR*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-ol 15. A solution of **11** (53mg, 0.129mmol) in dichloromethane/methanol 1:1 (1.3 mL) was cooled to 0 °C and added with $NaBH_4$ (20 mg, 0.516 mmol). After 15 min, dichloromethane (2.5 mL) and a 2% aqueous solution of AcOH (2.5 mL) were added, and the mixture was stirred at room temperature for 30 min. After separation, the aqueous layer was extracted with dichloromethane (3 x 10 mL), and the combined organic phases were dried ($MgSO_4$), filtered and concentrated under reduce pressure. Purification by silica gel chromatography (cyclohexane/ethyl acetate 4:1) gave alcohols **7** (18 mg, 34%) and **15** (30 mg, 57%) as colorless films. R_f = 0.44 (silica, cyclohexane/ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.52-7.29 (m, 10H, H_{Ar}), 5.79 (dddd, *J* = 16.8, 10.4, 8.2, 6.3 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.57 (s, 1H, H7), 5.19-5.11 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.96 (d, *J* = 11.4 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.78 (d, *J* = 11.4 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.33-4.28 (m, 1H, H6), 3.85 (t, *J* = 9.1 Hz, 1H, H3), 3.80-3.64 (m, 3H, H6, H5, H2), 3.59 (t, *J* = 9.1 Hz, 1H, H4), 3.30 (s, 3H, OMe), 2.63-2.49 (m, 2H, $\underline{CH_2}$-CH=CH_2), 2.26 (d, 1H, OH, *J* = 6.9Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 138.6 (Cq_{Ar}), 137.5 (Cq_{Ar}), 132.5 (CH_2-$\underline{CH}$=CH_2), 129.1 (C_{Ar}), 128.5 (C_{Ar}), 128.4 (C_{Ar}), 128.2 (C_{Ar}), 127.9 (C_{Ar}), 126.1 (C_{Ar}), 119.2 (CH_2-CH=$\underline{CH_2}$), 101.8 (C1), 101.3 (C7),

82.1 (C4), 79.5 (C3), 75.1 (O-$\underline{CH_2}$-Ph), 73.6 (C2), 69.1 (C6), 63.6 (C5), 47.9 (OMe), 37.2 ($\underline{CH_2}$-CH=CH_2); FT-IR (film): 3556, 2921, 2853, 1643, 1495, 1454, 1373, 1200, 1179, 1084, 986, 919, 763, 736, 697, 463 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{32}NO_6$ [M + NH_4]$^+$ 430.2230, found 430.2213; $[\alpha]_D^{20}$ = +56 ($CHCl_3$, c = 1.0);

(2*R*,4*aR*,6*R*,7*S*,8*R*,8*aR*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-ol 16. A solution of **12** (26 mg, 0.06 mmol) in THF (0.6 mL) was cooled to -78 °C and added drop-wise with a 1M solution of L-selectride in THF (0.3 mL, 0.30 mmol). After 20 min at -78 °C the mixture was quenched with methanol. Dichloromethane (5 mL) and Rochelle salts (1 M, 5 mL) were added, and after 18 h stirring at room temperature, the organic layer was separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduce pressure. After purification by silica gel chromatography (dichloromethane/acetonitrile 97:3), alcohol **16** was obtained as a colorless film (16 mg, 61%). R_f = 0.39 (silica, cyclohexane / ethyl acetate 3:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.52-7.28 (m, 10H, H_{Ar}), 5.70 (ddt, *J* = 17.1, 10.2, 7.1 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.59 (s, 1H, H7), 5.09-4.93 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.86 (d, *J* = 12.3 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.77 (d, *J* = 12.3 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.32-4.23 (m, 2H, H6, H4), 4.03-4.01 (m, 1H, H2), 3.85-3.76 (m, 2H, H3, H6), 3.52 (ddd, *J* = 10.5, 9.3, 4.7 Hz, 1H, H5), 3.41 (s, 3H, OMe), 2.90 (d, *J* = 2.7Hz, 1H, OH), 2.56-2.54 (m, 2H, $\underline{CH_2}$-CH=CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 138.1 (Cq_{Ar}), 137.6 (Cq_{Ar}), 131.8 (CH_2-$\underline{CH}$=CH_2), 129.1 (C_{Ar}), 128.6 (C_{Ar}), 128.4 (C_{Ar}), 128.2 (C_{Ar}), 127.9 (C_{Ar}), 126.2 (C_{Ar}), 119.2 (CH_2-CH=$\underline{CH_2}$), 101.7 (C7), 101.0 (C1), 79.4 (C4), 74.9 (C3), 73.1 (O-$\underline{CH_2}$-Ph), 69.69 (C6), 69.67 (C2), 65.6 (C5), 49.4 (OMe), 35.2 ($\underline{CH_2}$-CH=CH_2); FT-IR (film): 3527, 3070, 3031, 2922, 2853, 1728, 1640, 1496, 1454, 1373, 1314, 1274, 1210, 1176, 1093, 1028, 999, 918, 743,

696 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{32}NO_6$ $[M + NH_4]^+$ 430.2230, found 430.2240; $[\alpha]_D^{20}$ = + 15 ($CHCl_3$, c = 3.6).

*Preparation of quaternary methyl-α-D GlcNAc and ManNAc derivatives **17** and **18**.* A solution of **11** (48 mg, 0.116 mmol) and ammonium acetate (360 mg, 4.665 mmol) in THF / methanol (0.2 mL / 0.9 mL) was heated at 80 °C under microwave irradiation. After 10 min, $NaBH_3CN$ (74 mg, 1.165 mmol) was added and the solution was heated at 80 °C under microwave irradiation for 5 mn. After cooling to room temperature, dichloromethane (5 mL) and $NaHCO_3$ (5 mL) were added. After separation, the aqueous phase was extracted with dichloromethane (3 x 10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduce pressure. The residue was dissolved in dichloromethane (3 mL) and added with pyridine (190 µL, 2.33 mmol) and acetic anhydride (110 µL, 1.16 mmol). After 1 h, methanol (0.1 mL), dichloromethane (5 mL) and $NaHCO_3$ (5 mL) were added, and the phases were separated. The aqueous phase was extracted with dichloromethane (3 x 10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduce pressure. Purification by silica gel chromatography (chloroforme/methanol 99.5:0.5) gave **17** (20 mg, 38% over two steps) and **18** (17 mg, 33% over two steps) as colorless films. **N-((2*R*,4*aR*,6*S*,7*R*,8*R*,8*aS*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-yl)acetamide 17**: R_f = 0.33 (silica, chloroforme/methanol 99.5:0.5); ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.50-7.23 (m, 10H, H_{Ar}), 5.72 (ddt, *J* = 17.6, 9.6, 7.3 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.55 (s, 1H, H7), 5.41 (d, *J* = 10.2 Hz, 1H, NH), 5.19-5.04 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.86 (d, *J* = 12.3 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.61 (d, *J* = 12.3 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.28-4.22 (m, 2H, H2, H6), 3.78-3.57 (m, 4H, H6, H4, H3, H5), 3.20 (s, 3H, OMe), 2.45 (dd, *J* = 14.1, 7.3 Hz, 1H, $\underline{CH_2}$-CH=CH_2), 2.25 (dd, *J* = 14.1, 7.3 Hz, 1H, $\underline{CH_2}$-CH=CH_2), 1.86 (s, 3H, $\underline{CH_3}$-C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 169.4 (C=O),

138.8 (Cq_{Ar}), 137.5 (Cq_{Ar}), 131.4 (CH_2-$\underline{CH}$=CH_2), 129.1 (C_{Ar}), 128.38 (C_{Ar}), 128.36 (C_{Ar}), 128.1 (C_{Ar}), 127.6 (C_{Ar}), 126.1 (C_{Ar}), 119.3 (CH_2-CH=$\underline{CH_2}$), 102.2 (C1), 101.2 (C7), 82.5 (C4), 77.5 (C3), 74.1 (O-$\underline{CH_2}$-Ph), 69.0 (C6), 63.6 (C5), 54.1 (C2), 47.9 (OMe), 37.6 ($\underline{CH_2}$-CH=CH_2), 23.7 ($\underline{CH_3}$-C=O); FT-IR (film): 3286, 3065, 3033, 2923, 2856, 1656, 1515, 1498, 1371, 1313, 1213, 1172, 1087, 997, 915, 748, 696, 598, 478 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{32}NO_6$ $[M + H]^+$ 454.2230, found 454.2216; $[\alpha]_D^{20}$ = + 47 ($CHCl_3$, c =12.5). **N-((2*R*,4*aR*,6*S*,7*S*,8*R*,8*aS*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-yl)acetamide 18**: R_f = 0.28 (silica, chloroforme/methanol 99.5:0.5); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.44-7.15 (m, 10H, H_{Ar}), 5.68 (dddd, *J* = 17.0, 10.2, 7.6, 6.6 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.51 (s, 1H, H7), 5.47 (d, *J* = 10.8 Hz, 1H, NH), 5.10-4.99 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.75 (dd, *J* = 10.8, 4.5 Hz, 1H, H2), 4.69 (d, *J* = 12.0 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.47 (d, *J* = 12.0 Hz, 1H, O-$\underline{CH_2}$-Ph), 4.19 (dd, *J* = 9.0, 2.7 Hz, 1H, H6), 4.07 (dd, *J* = 9.6, 4.5 Hz, 1H, H3), 3.74-3.54 (m, 3H, H6, H4, H5), 3.15 (s, 3H, OMe), 2.46 (dd, *J* = 15.1, 7.6 Hz, 1H, $\underline{CH_2}$-CH=CH_2), 2.30 (dd, *J* = 15.1, 6.6 Hz, 1H, $\underline{CH_2}$-CH=CH_2), 1.98 (s, 3H, $\underline{CH_3}$-C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 169.7 (C=O), 138.3 (Cq_{Ar}), 137.3 (Cq_{Ar}), 130.7 (CH_2-$\underline{CH}$=CH_2) 128.9 (C_{Ar}), 128.3 (C_{Ar}), 128.2 (C_{Ar}), 127.9 (C_{Ar}), 127.5 (C_{Ar}), 126.1 (C_{Ar}), 119.4 (CH_2-CH=$\underline{CH_2}$), 103.4 (C1), 101.7 (C7), 78.5 (C4), 74.1 (C3), 71.4 (O-$\underline{CH_2}$-Ph), 68.9 (C6), 64.5 (C5), 50.6 (C2), 48.0 (OMe), 36.6 ($\underline{CH_2}$-CH=CH_2), 23.7 ($\underline{CH_3}$-C=O); FT-IR (film): 3358, 2960, 2922, 2852, 1654, 1538, 1455, 1374, 1260, 1091, 1016, 798, 696, 498 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{32}NO_6$ $[M + H]^+$ 454.2230, found 454.2243; $[\alpha]_D^{20}$ = 16 ($CHCl_3$, c = 2.3).

*Preparation of quaternary methyl-β-D GlcNAc and ManNAc derivatives **19** and **20**.*

A solution of **12** (65 mg, 0.158 mmol) and ammonium acetate (488 mg, 6.331 mmol) in THF / methanol (0.3 mL / 1.4 mL) was heated at 80 °C under microwave irradiation. After 10 min, $NaBH_3CN$ (98 mg, 1.58 mmol) was added and the solution was heated at

80 °C under microwave irradiation for 5 mn. After cooling to room temperature, dichloromethane (5 mL) and $NaHCO_3$ (5 mL) were added. After separation, the aqueous phase was extracted with dichloromethane (3 x 10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduce pressure. The residue was dissolved in dichloromethane (3 mL) and added with pyridine (256 µL, 3.166 mmol) and acetic anhydride (150 µL, 1.58 mmol). After 1 h, methanol (0.2 mL), dichloromethane (5 mL) and $NaHCO_3$ (5 mL) were added, and the phases were separated. The aqueous phase was extracted with dichloromethane (3 x 10 mL), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduce pressure. Purification by silica gel chromatography (dichloromethane/methanol from 96:4 to 93:7) gave **19** (23 mg, 32% over two steps) and **20** (21 mg, 29% over two steps) as colorless films. **N-((2*R*,4*aR*,6*R*,7*R*,8*R*,8*aS*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-yl)acetamide 19:** R_f = 0.33 (silica, dichloromethane/methanol 95:5); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.45-7.19 (m, 10H, H_{Ar}), 5.76 (ddt, *J* = 17.1, 10.1, 7.2 Hz, 1H, CH_2-CH=CH_2), 5.53 (s, 1H, H7), 5.08-4.99 (m, 3H, CH_2-CH=CH_2, NH), 4.86 (d, *J* = 12.4 Hz, 1H, O-CH_2-Ph), 4.66 (d, *J* = 12.4 Hz, 1H, O-CH_2-Ph), 4.41 (t, *J* = 9.2 Hz, 1H, H2), 4.23 (dd, *J* = 10.2, 4.8 Hz, 1H, H6), 3.85 (t, *J* = 9.3 Hz, 1H, H4), 3.69 (t, *J* = 10.2 Hz, 1H, H6), 3.57-3.44 (m, 2H, H3, H5), 3.34 (s, 3H, OMe), 2.44 (dd, *J* = 14.7, 7.2 Hz, 1H, CH_2-CH=CH_2), 2.35 (dd, *J* = 14.7, 7.2 Hz, 1H, CH_2-CH=CH_2), 1.87 (s, 3H, CH_3-C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 169.6 (C=O), 138.4 (Cq_{Ar}), 137.3 (Cq_{Ar}), 131.3 (CH_2-CH=CH_2), 129.1 (C_{Ar}), 128.5 (C_{Ar}), 128.4 (C_{Ar}), 128.3 (C_{Ar}), 127.9 (C_{Ar}), 126.1 (C_{Ar}), 118.6 (CH_2-CH=CH_2), 102.1 (C1), 101.3 (C7), 82.6 (C4), 77.9 (C3), 73.4 (O-CH_2-Ph), 69.4 (C6), 64.9 (C5), 52.5 (C2), 49.2 (OMe), 36.9 (CH_2-CH=CH_2), 23.7 (CH_3-C=O); FT-IR (film): 3285, 2961, 2924, 2853, 1651, 1514, 1454, 1371, 1312, 1260, 1216, 1092, 1053, 1016, 920, 800, 735, 696, 497 cm^{-1};

HRMS (ESI): m/z Calcd for $C_{24}H_{32}NO_6$ $[M + H]^+$ 454.2230, found 454.2227; $[\alpha]_D^{20}$ = + 15 ($CHCl_3$, c =3.7). **N-((2*R*,4*aR*,6*R*,7*S*,8*R*,8*aS*)-6-allyl-8-(benzyloxy)-6-methoxy-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-yl)acetamide 20:** R_f = 0.30 (silica, dichloromethane/methanol 95:5); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.45-7.28 (m, 10H, H_{Ar}), 5.98 (d, *J* = 9.9 Hz, 1H, NH), 5.75 (ddt, *J* = 17.2, 10.2, 7.5 Hz, 1H, CH_2-CH=CH_2), 5.54 (s, 1H, H7), 5.10-5.03 (m, 2H, CH_2-CH=CH_2), 4.75 (d, *J* = 12.0 Hz, 1H, O-CH_2-Ph), 4.69-4.62 (m, 2H, O-CH_2-Ph, H2), 4.39-4.30 (m, 1H, H6), 4.20-4.14 (m, 1H, H4), 3.95 (t, *J* = 6.9 Hz, 1H, H3), 3.69-3.66 (m, 2H, H6, H5), 3.32 (s, 3H, OMe), 2.57 (dd, *J* = 14.5, 7.5 Hz,

1H, $\underline{CH_2}$-CH=CH_2), 2.39 (dd, *J* = 14.5, 7.5 Hz, 1H, $\underline{CH_2}$-CH=CH_2), 1.95 (s, 3H, $\underline{CH_3}$-C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 168.8 (C=O), 137.1 (Cq_{Ar}), 136.4 (Cq_{Ar}), 130.9 (CH_2-$\underline{CH}$=CH_2), 128.1 (C_{Ar}), 127.5 (C_{Ar}), 127.4 (C_{Ar}), 127.1 (C_{Ar}), 126.9 (C_{Ar}), 125.2 (C_{Ar}), 117.6 (CH_2-CH=$\underline{CH}$), 100.7 (C1), 100.3 (C7), 80.2 (C4), 74.1 (C3), 72.9 (O-$\underline{CH_2}$-Ph), 69.0 (C6), 63.6 (C5), 49.3 (C2), 47.2 (OMe), 36.9 ($\underline{CH_2}$-CH=CH_2), 22.4 ($\underline{CH_3}$-C=O); FT-IR (film): 2962, 2922, 2852, 1632, 1464, 1260, 1093, 1018, 798, 695, 458 cm^{-1}; HRMS (ESI): m/z Calcd for $C_{24}H_{32}NO_6$ $[M + H]^+$ 454.2230, found 454.2228; $[\alpha]_D^{20}$ = + 11 ($CHCl_3$, c = 4.5);

(1*R*,2*R*,3*S*,4*S*,5*R*)-5-allyl-3-(benzyloxy)-6,8-dioxabicyclo[3.2.1]octane-2,4-diol 13. R_f = 0.17 (silica, cyclohexane/ethyl acetate 5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.39-7.31 (m, 5H, H_{Ar}), 5.87 (ddt, *J* = 17.2, 10.1, 7.3 Hz, 1H, CH_2-$\underline{CH}$=CH_2), 5.21-5.13 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.71 (d, *J* = 11.4 Hz, 1H, O-C$\underline{H_2}$-Ph), 4.59 (d, *J* = 11.4 Hz, 1H, O-C$\underline{H_2}$-Ph), 4.45 (d, *J* = 5.7 Hz, 1H, H2), 4.19 (d, *J* = 7.5 Hz, 1H, H6), 3.86-3.77 (m, 3H, H5, H6, H3), 3.67 (dd, *J* = 11.4, 6.0 Hz, 1H, H4), 3.04 (d, *J* = 11.4 Hz, 1H, OH), 2.73-2.59 (m, 2H, $\underline{CH_2}$-CH=CH_2), 2.36 (br d, 9.9 Hz, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 137.3 (Cq_{Ar}), 131.9 (CH_2-$\underline{CH}$=CH_2), 128.8 (C_{Ar}), 128.3 (C_{Ar}), 127.9 (C_{Ar}), 118.8 (CH_2-CH=$\underline{CH_2}$), 108.8 (C1), 78.8 (C3), 77.1 (C2), 74.1 (O-$\underline{CH_2}$-Ph), 69.6 (C5), 67.5 (C4), 65.9 (C6), 37.7 ($\underline{CH_2}$-CH=CH_2); FT-IR (film): 3427, 3073, 3034, 2897, 1718, 1642, 1454, 1400, 1207, 1063, 918, 796, 736, 696, 608, 460 cm^{-1}; $[\alpha]_D^{20}$ = - 10 ($CHCl_3$, c = 4.9).

(2*R*,4*aR*,6*R*)-6-allyl-8-hydroxy-6-methoxy-2-phenyl-4,4a-dihydropyrano[3,2-*d*][1,3]dioxin-7(6H)-one 14. R_f = 0.11 (silica, cyclohexane/ethyl acetate 5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.57-7.29 (m, 5H, H_{Ar}), 5.97-5.83 (m, 2H, H7, CH_2-$\underline{CH}$=CH_2), 5.63 (br s, 1H, OH), 5.22-5.16 (m, 2H, CH_2-CH=$\underline{CH_2}$), 4.82 (dd, *J* = 10.1, 6.8 Hz, 1H, H5), 4.51 (dd, *J* = 10.1, 6.8 Hz, 1H, H6), 3.96 (t, *J* = 10.1 Hz, 1H, H6), 3.34 (s, 3H, OMe), 2.71-2.55 (m, 2H, $\underline{CH_2}$-CH=CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 190.2 (C2), 148.0 (C3), 135.2 (Cq_{Ar}), 131.7 (C4), 130.4 (CH_2-$\underline{CH}$=CH_2), 130.2 (C_{Ar}), 128.7 (C_{Ar}), 126.5 (C_{Ar}), 119.7

(CH_2-CH=$\underline{CH_2}$), 103.3 (C7), 102.7 (C1), 69.0 (C6), 62.3 (C5), 51.9 (OMe), 38.3 ($\underline{CH_2}$-CH=CH_2).

Associated Content

The supporting Information is available free of charge on the ACS publications website. They include copy of the NMR spectra (^1H and ^{13}C) of **5**, **6**, **7**, **8**, **9**, **10**, **11**, **12**, **13**, **14**, **15**, **16**, **17**, **18**, **19**, **20**.

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The authors declare no competing financial interest.

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