Intra- and Intermolecular 1,3-Dipolar Cycloaddition of Sugar Ketonitrones with Mono-, Di- and Trisubstituted Dipolarophiles

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A) General Experimental Methods. All reactions were carried out under argon with the exclusion of moisture. All solvents for reaction and extraction were reagent grade. THF was distilled from sodium benzophenone ketyl; methylene chloride, pyridine and acetonitrile were distilled from calcium hydride. Except where indicated, the reagents purchased were used without further purification. Flash column chromatography was carried out on 230-400 mesh silica gel. 4 Å Molecular sieves were activated by heating in an oven at 400°C for 12 h, then cooled in a dessicator under vacuum.

B) Detailed experimental procedures for all cycloaddition precursors

4-*O*-Allyl-1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose (7a). A solution of 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose (**6**) (3 g, 14.76 mmol) in dry THF (10 mL) was added dropwise to a suspension of sodium hydride (405 mg, 16.23 mmol) in dry THF (10 mL) at 0 °C (previously prepared by washing 60% sodium hydride (675 mg) with 3 mL of THF). After 30 min, the cooling bath was removed and the reaction was allowed to warm up to rt. Then, allyl bromide (1.3 mL, 15.2 mmol) and *n*-Bu₄NI (100 mg) were added. After 16 h, a saturated NH₄Cl solution was added and the product was extracted with Et₂O. The ethereal extracts were dried over Na₂SO₄ and concentrated *in vacuo* to give **7a** (3.5 g, 98%). ¹H NMR (CDCl₃, 300 MHz) δ: 5.93 (tdd, *J*_{trans} = 17.2 Hz, *J*_{cis} = 10.3 Hz, *J* = 5.7 Hz, 1H, -O-CH₂-CH=CH₂), 5.36 (m, 1H, H1), 5.33 (m, *J*_{trans} = 17.2 Hz, *J*_{gem}~*J*_{al}~ 1.5 Hz, 1H, -O-CH₂-CH=CH₂), 5.24 (m, *J*_{cis} = 10.3 Hz, *J*_{gem} ≈ *J*_{al} = 1.5 Hz, 1H, -O-CH₂-CH=CH₂), 4.60 (m, 1H, H5), 4.22 (m, 1H, H3), 4.15 (m, 2H, -O-CH₂-CH=CH₂), 4.09 (dd, *J*_{4,3} = 6.4 Hz, *J*_{4,5} = 3.0 Hz, 1H, H2), 3.94 (dd, *J*_{gem} = 7.3 Hz, *J*_{6endo-5} = 1.3 Hz, 1H, H6endo), 3.76 (dd, *J*_{gem} = 7.3 Hz, *J*_{6exo-5} ≈ 7.3 Hz, 1H, H6exo), 3.64 (br s, 1H, H4), 1.53 (s, 3H, -CH₃), 1.33 (s, 3H, -CH₃). ¹³C NMR (CDCl₃, 75 MHz) δ: 134.0 (CH=CH₂), 118.0 (CH=CH₂), 109.8 (C(CH₃)₂), 99.2 (C1), 76.2, 73.8, 73.4 y 72.3 (C2, C3, C4, y C5), 70.7 (-O-CH₂-CH=CH₂), 64.5 (C6), 26.0 y 25.8 (C(CH₃)₂). MS (EI): 242 (100, M⁺), 142 (84), 57 (55). HRMS (EI): Calc. for C₁₂H₁₈O₅: 242.1154; Found: 242.2248.

4-*O*-Allyl-1,6-anhydro- β -D-mannopyranose (8a).¹ A solution of **7a** (223 mg, 0.92 mmol) in 20% aqueous acetic acid (3 mL) and THF (2 mL) was stirred at 60 °C for 23 h. Evaporation of the solvent *in vacuo* and removal of the last traces of water by distillation with toluene (3 mL) gave **8a** (221 mg, quantitative). ¹H NMR (CDCl₃, 300 MHz) δ : 5.92 (m, 1H, -O-CH₂-CH=CH₂), 5.37 (s, 1H, H1), 5.30 (m, $J_{\text{trans}} = 17.2$ Hz, 1H, -O-CH₂-CH=CH₂), 5.21 (m, $J_{\text{cis}} = 10.4$ Hz, 1H, -O-CH₂-CH=CH₂), 4.56 (m, 1H, H5), 4.13 (m, 3H, -O-CH₂-CH=CH₂, H6endo), 4.00 (m, 1H, H3), 3.72 (m, 2H, H2, H6exo), 3.57 (s, 1H, H4), 3.34 (br s, 2H, -OH, -OH). ¹³C NMR (CDCl₃, 75 MHz) δ : 134.2 (CH=CH₂), 117.9 (CH=CH₂), 101.6 (C1), 78.5, 74.1 (C4, C5), 70.8 (C6), 68.8, 66.8 (C2, C3), 64.8 (C7). MS (FAB⁺): 203 (M⁺⁺¹).

4-*O*-Allyl-1,6-anhydro-2-*O*-benzyl- β -D-mannopyranose (9a). A suspension of **8a** (370 mg, 1.82 mmol) and *n*-Bu₂SnO (470 mg, 1.88 mmol) in dry benzene (18 mL) was refluxed for 3 h, using a Dean-Stark trap to remove the generated water. The reaction mixture was diluted with benzene (8 mL) and allowed to warm up to rt. Benzyl bromide (240 mL, 1.9 mmol) and *n*-Bu₄NI (675 mg, 1.82 mmol) were added and stirring was continued at 90 °C for another 5 h. Flash chromatography (35%, 37%, 40% AcOEt-hexane mixtures) gave **9a** (284 mg, 53%). ¹H NMR (CDCl₃, 250 MHz) δ : 7.35 (m, 5H, ArH), 5.90 (tdd, $J_{\text{trans}} = 17.4$ Hz, $J_{\text{cis}} = 10.3$ Hz, $J = 5.6$ Hz, 1H, -O-CH₂-CH=CH₂), 5.41 (s, 1H, H1), 5.30 (m, $J_{\text{trans}} = 17.4$ Hz, $J_{\text{gem}} \sim J_{\text{al}} = 1.6$ Hz, 1H, -O-CH₂-CH=CH₂), 5.22 (m, $J_{\text{cis}} = 10.3$ Hz, $J_{\text{gem}} \sim J_{\text{al}} = 1.6$ Hz, 1H, -O-CH₂-CH=CH₂), 4.66 (AB_q, $J = 11.7$ Hz, $\Delta\delta = 0.11$, 2H, ArCH₂), 4.56 (m, 1H, H5), 4.23 (dd, $J_{6\text{endo}-6\text{exo}} = 7.0$ Hz, $J_{6\text{endo}-5} \sim 0.8$ Hz, 1H, H6endo), 4.2-4.0 (m, 3H, H3, -O-CH₂-CH=CH₂), 3.73 (dd, $J_{6\text{exo}-6\text{endo}} = 7.0$ Hz, $J_{6\text{exo}-5} = 5.9$ Hz, 1H, H6exo), 3.59 (m, 2H, H4 y H2), 3.11 (d, $J = 2.5$ Hz, 1H, OH). ¹³C NMR (CDCl₃, 75 MHz) δ : 137.2 (Ar_{ipso}), 134.3 (-CH=CH₂), 128.6 (C_{meta}), 128.2 (C_{para}), 128.0 (C_{orto}), 117.8 (-CH=CH₂), 100.1 (C1), 78.1, 74.3, 73.4 (C2, C3, C4), 71.1 (Ph-CH₂-), 70.8 (-O-CH₂-), 67.3 (C5), 64.9 (C6). MS (EI): 292 (0.01, M⁺), 203 (35, M⁺-C₇H₇), 91 (100, C₇H₇). MS (FAB⁺): 293 (M⁺⁺¹).

4-*O*-Allyl-1,6-anhydro-2-*O*-benzyl-3-oxo- β -D-arabino-hexopyranose (4a). Dess-Martin

periodinane (126 mg, 0.3 mmol) and *tert*-butanol (30 μ L, 0.32 mmol) were added to a solution of **9a** (67 mg, 0.23 mmol) in CH₃CN (1.1 mL). After stirring at rt for 16 h, the reaction mixture was diluted with ethyl ether and a saturated aqueous solution of NaHCO₃:Na₂S₂O₃ (1:1). The organic layer was washed with brine, dried over Na₂SO₄ and concentrated *in vacuo* to give ketone **4a** as an oil (62 mg, 92%). ¹H NMR (CDCl₃, 300 MHz) δ : 7.5-7.2 (m, 5H, ArH), 5.85 (tdd, $J_{\text{trans}} = 17.5$ Hz, $J_{\text{cis}} = 10.3$ Hz, $J \sim 5.4$ Hz, 1H, -O-CH₂-CH=CH₂), 5.58 (d, $J_{1-2} = 2.2$ Hz, 1H, H1), 5.4-5.2 (m, 2H, -O-CH₂-CH=CH₂), 4.93 (d, $J_{\text{gem}} = 12.1$ Hz, 1H, H10), 4.63 (d, $J_{\text{gem}} = 12.1$ Hz, 1H, H10'), 4.77 (m, 1H, H5), 4.21 (d, $J = 2.2$ Hz, 1H, H2*), 4.06 (tdd, $J_{\text{gem}} = 12.7$ Hz, $J = 5.3$ Hz, $J = 1.2$ Hz, 1H, -O-CH₂-CH=CH₂), 3.98 (tdd, $J = 12.7$ Hz, $J = 6.1$ Hz, $J = 1.1$ Hz, 1H, -O-CH₂-CH=CH₂), 3.83 (dd, $J_{\text{gem}} = 8.3$ Hz, $J_{6\text{exo}-5} = 5.6$ Hz, 1H, H6exo), 3.69 (m, 2H, H6endo, H4*). ¹³C NMR (CDCl₃, 75 MHz) δ : 202.6 (C3), 137.0 (Ar_{ipso}), 133.0 (CH=CH₂), 128.5 (C_{meta}), 128.4 (C_{para}), 128.2 (C_{orto}), 119.0 (CH=CH₂), 102.5 (C1), 83.1, 81.2 (C4, C2), 76.4 (C5), 73.1, 71.0 (-O-CH₂-, Ph-CH₂), 65.4 (C6). MS *m/z* (%): 290 (0.92, M⁺), 261 (0.85, M-(CH₂-O)⁺), 203, 197, 157, 125, 91 (100, C₇H₇), 65. IR : 2889 (O-CH₂-O), 1734 (C=O), 1454 (CH₂-C=C), 1105, 990, 742 Elem. Anal. Calc. for C₁₆H₁₈O₅: C, 66.202; H, 6.248. Found: C, 65.85; H, 6.21.

Ketones 4b and 4c. A solution of **4a** (261 mg) and DBU (147 μ L) in toluene (30 mL) was left for 22 h at rt. DBU was removed by filtration through a short pad of silica gel and the solvents were evaporated. Column chromatography (15% AcOEt-hexane) gave ketone **4b** (111 mg, 42%) and ketone **4c** (67 mg, 26%). **4b**: ¹H NMR (CDCl₃, 300 MHz) δ : 7.39-7.28 (m, 5H, ArH), 5.90 (tdd, $J_{\text{trans}} = 16.4$ Hz, $J_{\text{cis}} = 10.3$ Hz, $J \sim 5.6$ Hz, 1H, -O-CH₂-CH=CH₂), 5.52 (d, $J_{1-2} = 2.0$ Hz, 1H, H1), 5.27 (m, 2H, -O-CH₂-CH=CH₂), 4.75 (m, 1H, H5), 4.63 (d, $J_{\text{gem}} = 12.0$ Hz, 1H, H10), 4.51 (d, $J_{\text{gem}} = 12.0$ Hz, 1H, H10'), 4.33 (d, $J_{4-5} = 4.5$ Hz, 1H, H4), 4.32 (m, 1H, -O-CH₂-CH=CH₂), 4.05 (tdd, $J = 12.7$ Hz, $J = 6.2$ Hz, $J = 1.2$ Hz, 1H, -O-CH₂-CH=CH₂), 3.92 (m, $J_{6\text{endo}-6\text{exo}} = 7.9$ Hz, 1H, H6endo), 3.69 (d, $J_{2-1} = 2.0$ Hz, 1H, H2), 3.68 (m, $J_{6\text{endo}-6\text{exo}} = 7.9$ Hz, $J_{6\text{exo}-5} = 4.8$ Hz, 1H, H6exo). ¹³C NMR (CDCl₃, 75 MHz) δ

: 203.1 (C3), 136.6 (Ar_{ipso}), 133.6 ($\underline{\text{CH}}=\text{CH}_2$), 128.3 (C_{meta}), 128.3 (C_{para}), 128.3 (C_{orto}), 118.4 ($\text{CH}=\underline{\text{CH}}_2$), 101.6 (C1), 82.1, 79.1 (C4, C2), 75.1 (C5), 72.6, 72.5 (-O- $\underline{\text{CH}}_2$ -, Ph- $\underline{\text{CH}}_2$), 65.1 (C6). IR: 2893 (O-CH₂-O), 1741 (C=O), 1455 (CH₂-C=C), 1117, 1060. MS (EI): 290 (0.64, M⁺), 261 (0.33, M-(CH₂-O)⁺), 91 (100, C₇H₇). HRMS (EI): Calc. for C₁₆H₁₈O₅: 290.1154; Found: 290.1157. **4c**: ¹H NMR (CDCl₃, 300 MHz) δ : 7.39-7.27 (m, 5H, ArH), 5.91 (tdd, $J_{\text{trans}} = 16.7$ Hz, $J_{\text{cis}} = 10.4$ Hz, $J \sim 5.4$ Hz, 1H, -O-CH₂- $\underline{\text{CH}}=\text{CH}_2$), 5.56 (d, $J_{1-2} = 2.3$ Hz, 1H, H1), 5.34-5.22 (m, 2H, -O-CH₂-CH= $\underline{\text{CH}}_2$), 4.97 (d, $J_{\text{gem}} = 12.2$ Hz, 1H, H10), 4.72 (m, 1H, H5), 4.62 (d, $J_{\text{gem}} = 12.2$ Hz, 1H, H10'), 4.40 (tdd, $J_{\text{gem}} = 12.8$ Hz, $J = 5.3$ Hz, $J = 1.4$ Hz, 1H, -O- $\underline{\text{CH}}_2$ -CH=CH₂), 4.14-4.04 (m, 3H, H₄, H_{6endo}, H7), 3.94 (m, $J_{2-1} = 2.3$ Hz, $J_{2-4} = 3.8$ Hz, 1H, H2), 3.80 (dd, $J_{\text{gem}} = 8.0$ Hz, $J_{6\text{exo}-5} = 5.0$ Hz, 1H, H6exo). ¹³C NMR (CDCl₃, 75 MHz) δ : 202.7 (C3), 137.2 (Ar_{ipso}), 133.7 ($\underline{\text{CH}}=\text{CH}_2$), 128.5 (C_{meta}), 128.1 (C_{para}), 128.0 (C_{orto}), 118.4 ($\text{CH}=\underline{\text{CH}}_2$), 102.4 (C1), 82.1, 80.2 (C4, C2), 75.5 (C5), 73.0, 72.4 (-O- $\underline{\text{CH}}_2$ -, Ph- $\underline{\text{CH}}_2$), 66.6 (C6). MS (EI): 290 (0.12, M⁺), 91 (100, C₇H₇). HRMS (EI): Calc. for C₁₆H₁₈O₅: 290.1154; Found: 290.1154.

1,6-Anhydro-4-O-benzoyl-2,3-isopropylidene- β -D-mannopyranose (7b).² To a cold (0°C) solution of **6** (2.0 g, 9.89 mmol) in dry Py (10 mL), BzCl (1.23 mL, 10.38 mmol, 105 mol%) and DMAP (cat.) were added, and the reaction mixture was allowed to warm up slowly to rt. When no starting material was detected by tlc (AcOEt-hexane, 10:90, R_{f alcohol} = 0.38), the reaction mixture was diluted with ethyl ether (30 mL) and washed with solutions of NaHCO₃(dil) and CuSO₄ (5%; 100 mL). Drying over Na₂SO₄ and evaporation of the solvent, afforded **7b** (3.0 g, 99%) as white crystals (AcOEt, mp = 134°C). ¹H NMR (CDCl₃, 300 MHz) δ : 8.09 (m, 2H; ArH_{orto}), 7.60 (m, 1H; ArH_{para}), 7.46 (m, 2H; ArH_{meta}), 5.43 (d, $J_{4,5} = 2.6$ Hz, 1H; H4), 5.27 (s, 1H; H1), 4.70 (m, 1H; H3 or H2), 4.30 (m, 1H; H5), 4.15 (m, 2H; H2 or H3, H6endo), 3.83 (dd, $J_{6,6'} \approx J_{6\text{exo},5} \approx 7$ Hz, 1H; H6exo), 1.58 [s, 3H; C(CH₃)₂], 1.34 [s, 3H; C(CH₃)₂]. ¹³C NMR (CDCl₃, 75 MHz) δ : 165.4 (PhCO), 133.5 (Ar, C_{para}), 129.8 (Ar, C_{orto}), 129.3 (Ar, C_{ipso}), 128.5 (Ar, C_{meta}), 110.3 [$\underline{\text{C}}(\text{CH}_3)_2$], 99.3 (C1), 74.1, 73.3, 72.2, 71.4 (C2, C3,

C4, C5), 64.7 (C6), 25.9, 25.8 [C(CH₃)₂]. IR (KBr): 1710 cm⁻¹ (PhCOO). MS *m/z* (%): 291 [9, (M-CH₃)⁺], 248, 184, 139, 127, 105 [100, (PhCO)⁺], 77 (32, Ph⁺), 43.

1,6-Anhydro-4-*O*-benzoyl- β -D-mannopyranose (8b).² A suspension of **7b** (2.90 g, 9.6 mmol) in aqueous AcOH (30%, 125 mL) was refluxed in a 250 mL one-necked round-bottomed flask fitted with a reflux condenser. When no starting material was left (tlc, AcOEt-hexane, 10:90), the solvent was evaporated and the last traces of acid and water were removed by azeotropic distillation with toluene (3 x 50 mL) to give **8b** (2.55 g, quant.) as a white powder (AcOEt, m.p.= 134°C). ¹H NMR (CDCl₃, 250 MHz) δ : 8.06 (m, 2H; ArH_{orto}), 7.60 (m, 1H; ArH_{para}), 7.46 (m, 2H; ArH_{meta}), 5.48 (s, 1H; H4), 5.18 (s, 1H; H1), 4.70 (m, 1H; H5), 4.34 (d, $J_{6,6'} = 7.5$ Hz 1H; H6_{endo}), 4.13 (m, 1H; H3), 3.83 (m, 2H; H2, H6_{exo}), 3.26 (d, $J_{OH,3} = 4.9$ Hz, 1H; C₃OH), 3.06 (d, $J_{OH,2} = 7.1$ Hz, 1H; C₂OH). ¹³C NMR (CD₃Cl-CD₃OD, 4:1, 63 MHz) δ : 166.0 (PhCO), 133.4 (Ar, C_{para}), 129.6 (Ar, C_{orto}), 129.3 (Ar, C_{ipso}), 128.4 (Ar, C_{meta}), 101.7 (C1), 74.0, 73.6 (C4, C5), 68.1, 66.2 (C2, C3), 64.7 (C6). MS *m/z* (%): 123 [19, (PhCO₂)⁺], 106, 105 [100, (PhCO)⁺], 77 (29, Ph⁺), 70, 60, 51. Anal. calcd. for (C₁₃H₁₄O₆): 58.65 (%C), 5.31 (%H). Found: 58.42 (%C), 5.60 (%H).

2-*O*-Allyl-1,6-anhydro-4-*O*-benzoyl- β -D-mannopyranose (9b). A mixture of **8b** (3.0 g, 11.27 mmol) and *n*-Bu₂SnO (3.0 g, 11.83 mmol, 105 mol%) in dry benzene (150 mL), was refluxed for 2h with azeotropic removal of water. The resulting homogeneous solution was cooled to rt, allyl bromide (3.23 mL, 36.63 mmol, 325 mol%) and *n*-Bu₄NI (3.19 g, 8.45 mmol, 75 mol%) were added, and the reaction mixture was warmed up again to reflux until no starting material was left (MeOH-CH₂Cl₂, 1:99). The solvent was removed under vacuum and the resulting oily residue was filtered through a path of silica using AcOEt-hexane mixtures as eluents. Further purification was done by stirring a solution of the product in ethyl ether with a 10% aqueous solution of KF for 24h. The organic layer was dried and filtered. Elimination of the solvents afforded the **9b** (2.92 g, 85%) as a slightly yellow oil. ¹H NMR (CDCl₃, 250 MHz) δ : 8.07 (m, 2H; ArH_{orto}), 7.59 (m, 1H; ArH_{para}), 7.46 (m, 2H; ArH_{meta}), 5.95 (m, 1H;

H8), 5.52 (br s, 1H; H1), 5.4-5.1 (m, 3H; H9_{cis}, H9_{trans}, H4), 4.70 (m, 1H; H5), 4.39 (d, $J_{6,6'} = 7.3$ Hz, 1H; H6_{endo}), 4.3-4.0 (m, 3H; H3, H7), 3.80 (dd, $J_{6,6'} = 7.3$ Hz, $J_{6\text{exo},5} = 5.8$ Hz, 1H; H6_{exo}), 3.63 (dd, $J_{2,3} = 5.1$ Hz, $J_{2,1} = 1.8$ Hz, 1H; H2), 3.19 (d, $J_{\text{OH},3} = 2.3$ Hz, 1H; OH). ^{13}C NMR (CDCl_3 , 63 MHz) δ : 165.4 (Ph COO^-), 133.8 (C8), 133.4 (Ar, C_{para}), 129.8 (Ar, C_{orto}), 129.3 (Ar, C_{ipso}), 128.5 (Ar, C_{meta}), 118.3 (C9), 100.2 (C1), 74.1 (C4), 73.3 and 73.2 (C3, C5), 70.3 (C7), 67.6 (C2), 65.2 (C6). MS m/z (%): 265 [6, (M-C₃H₅)⁺], 218, 217, 105 [100, (PhCO)⁺], 99, 77 (22, Ph⁺), 71.

2-O-Allyl-1,6-anhydro-4-O-benzoyl-3-oxo- β -D-arabino-hexopyranose (4d). To a solution of **9b** (1.07 g, 3.49 mmol) in dry acetonitrile (16 mL) magnetically stirred under Ar at rt, Dess-Martin periodinane (2.22 g, 5.23 mmol, 150 mol%) and *t*-BuOH (4.01 mmol, 0.37 mL, 115 mol%) were added. The consumption of the starting material was monitored by tlc (AcOEt-hexane, 25:75), the reaction mixture was diluted with ethyl ether and washed thoroughly with a 1/1 saturated solution of NaHCO₃-Na₂S₂O₃ and brine. Drying over Na₂SO₄, filtration and removal of the solvents under reduced pressure, afforded ketone **4d** (1.02 g, 96%), which was used in the dipolar cycloadditions reactions without further purification. ^1H NMR (CDCl_3 , 250 MHz) δ : 8.04 (m, 2H; ArH_{orto}), 7.60 (m, 1H; ArH_{para}), 7.47 (m, 2H; ArH_{meta}), 5.95 (m, 1H; H8), 5.73 (d, $J_{1,2} = 2.3$ Hz, 1H; H1), 5.4-5.2 (m, 3H; H9, H4), 5.02 (m, 1H; H5), 4.44 (ddt, 1H; H7), 4.27 (d, $J_{2,1} = 2.3$ Hz, 1H; H2), 4.15 (ddt, 1H; H7'), 3.95 (dd, $J_{6,6'} = 8.5$ Hz, $J_{6\text{exo},5} = 5.3$ Hz, 1H; H6_{exo}), 3.88 (dd, $J_{6,6'} = 8.5$ Hz, $J_{6\text{endo},5} = 1.4$ Hz, 1H; H6_{endo}). ^{13}C NMR (CDCl_3 , 63 MHz) δ : 199.2 (C3), 165.1 (Ph CO), 133.9, 133.8 (Ar, C_{para}, C8), 130.0 (Ar, C_{orto}), 128.7 (Ar, C_{meta}), 118.5 (C9), 102.6 (C1), 81.9, 78.1, 75.6 (C2, C4, C5), 72.5 (C7), 65.7 (C6). IR (film, NaCl): 3070, 2975, 2905, 2880, 1750 (Ph COO^-), 1730 (CO, ketone), 1605, 1460, 1325, 1265, 1185, 1120, 1100, 1075 cm^{-1} . MS m/z (%): 263 [5, (M-C₃H₅)⁺], 217, 105 [100, (PhCO)⁺], 77 (Ph⁺; 16), 51.

3-N-Allylamino-1,6-anhydro-2-O-benzyl-3-deoxy- β -D-mannopyranose (12). A solution of 1,6:3,4-dianhydro-2-O-benzyl- β -D-altropyranose (**11**) (568 mg, 2.43 mmol) and allylamine (3.6 mL, 48.53 mmol) in 1 mL of DMF was heated in a sealed tube at 120 °C for 4 days. The solvent was

evaporated *in vacuo* and the crude residue was partitioned between Et₂O and water. The organic extracts were dried over Na₂SO₄ and chromatographed to give **12** (450 mg, 65%). ¹H NMR (CDCl₃, 300 MHz) δ : 7.4-7.27 (m, 5H, ArH), 5.84 (m, 1H, H8), 5.40 (s, 1H, H1), 5.24-5.0 (m, 2H, H9, H9'), 4.62 (d, $J_{6\text{endo}-5} = 7.0$ Hz, 1H, H6endo), 4.55 (m, 2H, H10, H10), 4.43 (m, 1H, H5), 3.74-3.65 (m, 3H, H6exo, H4, H2), 3.29 (dd, 1H, H7), 3.12 (dd, 1H, H7). ¹³C NMR (CDCl₃, 75 MHz) δ : 137.0 (C_{ipso}), 136.0 (C8), 128 (C_{meta}), 127 (C_{para}), 126 (C_{orto}), 115 (C9), 100 (C1), 76 (C5), 73, 70 (C2,C4), 71 (C10), 65 (C6), 59 (C3), 52 (C7). IR: 3358, 2891, 1669, 1091. MS (FAB⁺): 293 (15, M⁺+2), 292 (77.7, M⁺+1), 282 (100). HRMS (FAB⁺) Calc. for C₁₆H₂₂NO₄: 292.1548. Found: 292.1546.

4-*O*-Acetyl-3-(*N*-Acetyl-*N*-Allylamino)-1,6-anhydro-2-*O*-benzyl-3-deoxy- β -D-mannopyranose

(13). A solution of **12** (330 mg, 1.13 mmol), Et₃N (860 μ L, 6.2 mmol), Ac₂O (530 μ L, 5.6 mmol) and DMAP (14 mg, 0.11 mmol) in AcOEt (1 mL) was left for 3 days at rt. Removal of the solvent *in vacuo* and chromatography (silica gel, 40%, 80% AcOEt-hexane), gave the diacetyl derivative (398 mg, 91%). ¹H NMR (CDCl₃, 300 MHz) δ : 7.37-7.25 (m, 5H, ArH), 5.67 (tdd, $J_{\text{trans}} = 19.4$ Hz, $J_{\text{cis}} = 10.4$ Hz, $J_{\text{vic}} = 4.1$ Hz, 1H, H8), 5.58 (m, $J_{1,2} = 5.0$ Hz, 1H, H1), 5.13-5.03 (m, 3H, H9, H9', H4*), 4.67 (m, 2H, H3*, H6exo, H10), 4.45 (dd, $J_{5-6\text{exo}} = 6.0$ Hz, $J = 1.6$ Hz, 1H, H5), 4.34 (d, $J_{\text{gem}} = 11.3$ Hz, 1H, H10'), 4.12-3.88 (m, 5H, H6exo, H6endo, H2, H7, H7'), 2.06 (s, 3H, CH₃), 2.02 (s, 3H, CH₃). ¹³C NMR (CDCl₃, 75 MHz) δ : 172.5 (-O-CO-CH₃), 170.9 (-N-CO-CH₃), 137.7 (C_{ipso}), 134.4 (C8), 128.5 (C_{meta}), 127.9 (C_{para}), 127.8 (C_{orto}), 115.3 (C9), 98.7 (C1), 76.7 (C5), 74.3, 73.7 (C2,C4), 72.9 (C10), 67.9 (C6), 50.2 (C3), 49.1 (C7), 22.0 (CH₃), 21.1 (CH₃). IR: 3427, 2963, 1733 (-O-CO-CH₃), 1642 (-N-CO-CH₃), 1394, 1109, 1027 cm⁻¹. MS (EI): 332 (3.95, M⁺-CH₃C=O), 284 (5.75, M⁺-C₇H₇), 91 (100, C₇H₇). MS (FAB⁺): 377 (17.5, M⁺+2), 376 (68.5, M⁺+1), 282 (100). HRMS (FAB⁺) calc. for C₂₀H₂₆NO₆: 376.1760; Found: 376.1762.

3-(*N*-Acetyl-*N*-Allylamino)-1,6-anhydro-2-*O*-benzyl-3-deoxy- β -D-mannopyranose (14).

K₂CO₃ (14 mg, 0.1 mmol) was added to a solution of **13** (35 mg, 0.09 mmol) in methanol (0.5 mL).

After 45 min, the solvent was removed *in vacuo* and the crude residue was partitioned between water and CH₂Cl₂. The organic layer was dried over Na₂SO₄ and evaporated to give **14** (30 mg, 98%), which was used without further purification. ¹H NMR (CDCl₃, 300 MHz) δ : 7.31-7.26 (m, 5H, ArH), 5.88 (m, 1H, H8), 5.57 (d, J = 4.52 Hz 1H, H1), 5.14 (m, 2H, H9, H9'), 4.83 (m, 1H, H3), 4.63 (d, J_{gem} = 11.1 Hz, 1H, H10), 4.58 (d, J = 5.9 Hz, 1H, H5), 4.32 (d, J = 11.1 Hz, 1H, H10'), 4.15 (dd, J = 8.6 Hz, J = 2.4 Hz, 1H, H7), 3.98 (m, 2H, H2, H7'), 3.90-3.77 (m, 3H, H6endo, H6exo, OH), 3.73 (m, 1H, H4), 2.08 (s, 3H, CH₃). ¹³C NMR (CDCl₃, 75 MHz) δ : 173.3 (-N-CO-CH₃), 137.9 (C_{ipso}), 135.4 (C8), 128.3 (C_{meta}), 127.7 (C_{para}), 127.7 (C_{orto}), 115.9 (C9), 98.7 (C1), 79.3 (C5), 74.5 (C4*), 72.8 (C10), 72.2 (C2*), 68.2 (C6), 54.5 (C3), 49.5 (C7), 22.2 (CH₃). IR: 3417 (-OH), 2970, 2929, 1627 (-N-CO-) cm⁻¹. MS (FAB⁺): 336 (7.9, M⁺+3), 335 (41, M⁺+2), 334 (100, M⁺+1). HRMS (FAB⁺): calc. for C₁₈H₂₄NO₅: 334.1654; Found: 334.1655.

3-(N-Acetyl-N-Allylamino)-1,6-anhydro-2-O-benzyl-3-keto- β -D-lyxopyranose (4e). It was obtained from **14** (112 mg, 0.34 mmol), PCC (290 mg, 1.35 mmol) and molecular sieves (170 mg) as described for **4f**. Chromatography (silica gel, gradient 50% ---> 70% AcOEt-hexane) gave **4e** (60 mg, 55%). ¹H NMR (CDCl₃, 300 MHz) δ : 7.40-7.29 (m, 5H, ArH), 5.76 (tdd, J_{trans} = 17.1 Hz, J_{cis} = 10.3 Hz, J_{vic} = 4.7 Hz, 1H, H8), 5.63 (d, $J_{1,2}$ = 1.8 Hz, 1H, H1), 5.33 (dd, J_{trans} = 17.1 Hz, J_{gem} = 1.3 Hz, 1H, H9), 5.18 (dd, J_{cis} = 10.3 Hz, J_{gem} = 1.3 Hz, 1H, H9'), 4.70 (d, J_{gem} = 11.9 Hz, 1H, H10), 4.64 (dd, $J_{5-6\text{exo}}$ = 4.0 Hz, J = 2.0 Hz, 1H, H5), 4.55 (d, J_{gem} = 11.9 Hz, 1H, H10'), 4.21 (d, $J_{6\text{endo}-6\text{exo}}$ = 8.1 Hz, 1H, H6endo), 4.0-3.89 (m, 4H, H2, H3, H7, H6exo), 3.73 (dd, J_{gem} = 17.1 Hz, J_{7-8} = 6.2 Hz, 1H, H7'), 1.98 (s, 3H, CH₃). ¹³C NMR (CDCl₃, 75 MHz) δ : 197.0 (C4), (C=O), 137.5 (C_{ipso}), 132.7 (C8), 128.6 (C_{meta}), 128.2 (C_{para}), 128.2 (C_{orto}), 118.0 (C9), 100.1 (C1), 81.9 (C5), 78.5 (C2), 72.8 (C10), 67.6 (C6), 65.2 (C3), 53.7 (C7), 21.3 (CH₃). IR: 3417, 2970, 2929, 1627 (-N-CO-) cm⁻¹. MS (FAB⁺): 334 (4, M⁺+3), 333 (20, M⁺+2), 332 (81, M⁺+1), 282 (100). HRMS (FAB⁺): calc. for C₁₈H₂₂NO₅: 332.14979; Found: 332.1503.

1,6-Anhydro-2,3-isopropylidene-4-oxo-*lyxo*-hexopyranose (4f). A solution of 1,6-anhydro-2,3-isopropylidene- β -D-mannopyranose (**6**) (1.5 g, 7.42 mmol) in CH₂Cl₂ (15 mL), was added dropwise to a stirred suspension of PCC (6.4 g, 29.7 mmol) and molecular sieves (4 Å, 3.7 g) in methylene chloride (10 mL). After 17 h, the reaction mixture was diluted with Et₂O, and the solid residue was decanted and washed with more Et₂O. Filtration through silica gel (100% diethyl ether) gave **4f** (1.25 g, 84%). ¹H NMR (CDCl₃, 300 MHz) δ 5.64 (d, J_{1-2} = 3.2 Hz, 1H, H1), 4.59 (m, 1H, H5), 4.55-4.40 (m, 2H, H2, H3), 4.04 (d, $J_{6\text{endo}-6\text{exo}}$ = 7.9 Hz, 1H, H6endo), 3.90 (dd, $J_{6\text{exo}-6\text{endo}}$ = 7.9 Hz, $J_{6\text{exo}-5}$ = 5.7 Hz, 1H, H6exo), 1.52 (s, 3H, CH₃), 1.36 (s, 3H, CH₃). ¹³C NMR (CDCl₃, 75 MHz) δ : 201.5 (C4), 113.5 (C(CH₃)₂), 99.8 (C1), 77.4, 76.8, 76.0 (C2, C3, C5), 67.5 (C6), 26.6, 25.9 (CH₃, CH₃). MS (EI): 200 (0.1, M⁺), 185 (84, M⁺-CH₃), 85 (100).

Nitrone 5f. MeNHOH.HCl (1.2 g, 14.36 mmol) was added to a solution of ketone **4f** (954 mg, 4.78 mmol) in pyridine (15 mL) at 5 °C . After 5 h, the solvent was removed *in vacuo* and the crude residue was filtered through silica gel (AcOEt 100%). Final washing with hexane gave nitrone **5f** as a white solid (1.06 g, 97%). ¹H NMR (CDCl₃, 500 MHz) δ : 5.79 (d, $J_{5-6\text{exo}}$ = 4.8 Hz, 1H, H5), 5.47 (d, J_{1-2} = 2.9 Hz, 1H, H1), 4.96 (d, J_{3-2} = 7.2 Hz, 1H, H3), 4.26 (dd, J_{2-1} = 2.9 Hz, J_{2-3} = 7.2 Hz, 1H, H2), 3.94 (d, $J_{6\text{endo}-6\text{exo}}$ = 7.4 Hz, 1H, H6endo), 3.86 (dd, $J_{6\text{exo}-6\text{endo}}$ = 7.4 Hz, $J_{6\text{exo}-5}$ = 4.8 Hz, 1H, H6exo), 3.81 (s, 3H, N-CH₃), 1.51 (s, 3H, CH₃), 1.38 (s, 3H, CH₃). ¹³C NMR (CDCl₃, 125 MHz,) δ : 141.5 (C4), 111.9 (C(CH₃)₂), 98.5 (C1), 75.2 (C2), 69.3 (C5), 69.1 (C3), 68.2 (C6), 48.3 (CH₃-N), 26.2, 25.7 (CH₃, CH₃). IR: 1592, 1380, 1081. MS (EI): 229 (36, M⁺), 184 (100, M⁺-(-O-N⁺-Me)). HRMS (EI) calc. for C₁₀H₁₅NO₅: 229.0950; Found: 229.0949.

Nitrone 5g. MeNHOH.HCl (515 mg, 6.15 mmol) was added to a mixture of ketone **4g** (530 mg, 2.05 mmol) and sodium acetate (505 mg, 6.15 mmol) in benzene (5 mL) at rt. After 3 h, the mixture was filtered through celite and the solvent was removed *in vacuo*. The crude residue was dissolved in CH₂Cl₂, washed with water and purified by column chromatography (silica gel, Ø=1 cm, L=12 cm,

AcOEt/hexane 50/50, 100%) to give the nitrone **5g** (419 mg, 71%). ¹H NMR (250 MHz, CDCl₃) δ : 6.06 (d, *J*=4.5, 1H, H₁), 5.34 (m, 1H, H₄), 5.13 (d, *J*=4.5, 1H, H₂), 4.50 (td, *J*=6.8, *J*=1.7, 1H, H₅), 4.19 (dd, *J*=8.7, *J*=6.8, 1H, H₆), 3.95 (dd, *J*=8.7, *J*=7.0, 1H, H_{6'}), 3.83 (s, 3H, CH₃), 1.42 (s, 3H, CH₃), 1.40 (s, 3H, CH₃), 1.33 (s, 3H, CH₃), 1.29 (s, 3H, CH₃). ¹³C-NMR (75.4 MHz, CDCl₃) δ : 143.7 (C=N), 114.0 (C), 109.2 (C), 105.7 (C₁), 79.4, 78.5, 77.8 (C₅, C₄, C₂), 64.8 (C₆), 50.3 (CH₃), 27.4, 27.2, 26.1, 25.0 (CH₃, CH₃, CH₃, CH₃). MS (IE): 287 (0.64, M⁺), 272 (11.2, M⁺-CH₃), 187 (92.8), 129 (100), 84 (65).

Nitron 5h. MeNHOH.HCl (470 mg, 5.6 mmol) was added to a mixture of ketone **4h** (200 mg, 0.93 mmol), molecular sieves (4 Å, 200 mg) and pyridine ((300 μ L, 3.7 mmol) in ethanol (5 mL). After 2.5 h at 50° C, the mixture was filtered through celite and the solvent was removed *in vacuo*. The crude residue was dissolved in CH₂Cl₂, washed with water and purified by column chromatography (silica gel, $\varnothing$ =1 cm, L=12 cm, AcOEt/hexane 40/60) to give the nitron **5h** (192 mg, 85%). ¹H-NMR (250 MHz, CDCl₃) δ : 6.0 (d, *J*=3.6, 1H, H₁), 5.73 (d, *J*=4.8, 1H, H₄), 4.88 (d, *J*=4.8, 1H, H₃), 4.85 (d, *J*=3.6, 1H, H₂), 1.54 (s, 3H, CH₃), 1.37 (s, 3H, CH₃). ¹³C-NMR (62.9 MHz, CDCl₃) δ : 161.0 (C₆), 133.6 (C₅), 113.9 (C), 106.8 (C₁), 83.2, 81.5, 75.8 (C₂, C₃, C₄), 51.4 (N-CH₃), 27.5, 26.8 (CH₃, CH₃). MS (IE): 244 (0.6, M⁺+1), 243 (2.8, M⁺), 228 (100, M⁺-CH₃), 168 (86.9). HRMS (IE) calc. for C₁₀H₁₃NO₆: 243.0743; Found: 243.0751.

3-O-Allyl-1,2-5,6-diisopropylidene- β -D-glucofuranose (16a).³ It was prepared (1.13 g, 98%), according to the procedure reported above for **7a**, from **15** (1 g, 3.84 mmol), sodium hydride (100 mg, 4.22 mmol), allyl bromide (365 μ L, 4.22 mmol) and *n*-Bu₄NI (28 mg, 0.07 mmol).

1,2-5,6-O-diisopropylidene-3-O-(2-methyl-2-propenyl)- β -D-glucofuranose (16b).⁴ It was prepared (1.2 g, 99%) from **15** (1 g, 3.84 mmol), sodium hydride (100 mg, 4.22 mmol), 2-methyl-3-bromo-1-propene (400 μ L, 3.95 mmol) and *n*-Bu₄NI (28 mg), according to the procedure described for **7a**. ¹H-NMR (250 MHz, CDCl₃) δ : 5.88 (m, 1H, H₁), 4.99 (m, 1H, =CH₂), 4.91 (m, 1H, =CH₂), 4.54 (m, 1H, H₂), 4.32 (m, 1H, H₅), 4.13-3.92 (m, 6H, H₃, H₄, H₆, H_{6'}, CH₂), 1.75 (s, 3H, -CH₃), 1.49 (s, 3H, -

CH₃), 1.41 (s, 3H, -CH₃), 1.34 (s, 3H, -CH₃), 1.31 (s, 3H, -CH₃). ¹³C-NMR (62.9 MHz, CDCl₃) δ : 141.3 (C=), 112.6 (CH₂=), 111.4 (C(CH₃)₂), 108.7 (C(CH₃)₂), 105.0 (C₁), 82.3, 81.0, 79.9 (C₂, C₃, C₄), 73.9 (CH₂), 72.1 (C₅), 67.2 (CH₂), 26.6, 26.5, 26.0, 25.2, 19.2 (CH₃, CH₃, CH₃, CH₃, CH₃). MS (EI): 314 (22, M⁺), 299 (100, M⁺-CH₃), 241 (48), 155 (44). HRMS (EI) calc. for C₁₆H₂₆O₆: 314.1729; Found: 314.1723.

1,2-5,6-*O*-diisopropyliden-3-*O*-(2-methyl-1-propenyl)-β-D-glucofuranose (16c).⁴ Potassium *tert*-butoxyde (470 mg, 3.84 mmol) was added to a solution of **16b** (3.84 mmol) in DMSO (20 mL). After stirring at 100 °C for 20 h, the reaction mixture was diluted with ethyl ether and water. The organic layer was washed several times with water, dried over sodium sulphate and concentrated *in vacuo*. Column chromatography (AcOEt-hexane 10-90) gave **16c** as an oil (940 mg, 78%). ¹H-NMR (250 MHz, CDCl₃) δ : 5.88 (m, 2H, H₁, CH=), 4.53 (d, *J*=3.7, 1H, H₂), 4.33 (m, 1H, H₅), 4.19-4.00 (m, 4H, H₃, H₄, H₆, H_{6'}), 1.57 (s, 3H, -CH₃), 1.55 (s, 3H, -CH₃), 1.50 (s, 3H, -CH₃), 1.43 (s, 3H, -CH₃), 1.34 (s, 3H, -CH₃), 1.31 (s, 3H, -CH₃). ¹³C-NMR (62.9 MHz, CDCl₃) δ : 138.2 (CH=), 113.0 (C=), 111.8 (C(CH₃)₂), 108.9 (C(CH₃)₂), 105.1 (C₁), 82.6, 82.6, 80.7 (C₂, C₃, C₄), 72.3 (C₅), 65.8 (C₆), 29.6, 29.6, 26.7, 26.2, 19.3, 15.0 (CH₃, CH₃, CH₃, CH₃, CH₃, CH₃). MS (EI) 314 (95, M⁺), 299 (84, M⁺-CH₃), 241 (56), 101 (100). HRMS (EI) calc. for C₁₆H₂₆O₆: 314.1729; Found: 314.1728.

3-*O*-Allyl-1,2-isopropylidene-β-D-glucofuranose (17a).³ A solution of **16a** (892 mg, 2.97 mmol) in 9 mL of 33% acetic acid and 2 mL of THF was stirred at 60 °C for 7 h. Evaporation of the solvent *in vacuo* and removal of the last traces of water by distillation with toluene (3 mL) gave **17a** (867 mg, quantitative). ¹H NMR (CDCl₃, 250 MHz) δ : 5.91 (d, *J*₁₋₂ = 3.7 Hz, 1H, H₁), 5.90 (m, 1H, -O-CH₂-CH=CH₂), 5.31 (m, *J*_{trans} ~ 17.1 Hz, 1H, -O-CH₂-CH=CH₂), 5.22 (m, *J*_{cis} ~ 10.3 Hz, 1H, -O-CH₂-CH=CH₂), 4.57 (d, *J* = 3.7 Hz, 1H, H₂), 4.3-3.9 (m, 5H, H₃, H₄, H₅, H₆), 3.83 (dd, *J*_{6-6'} = 11.4 Hz, *J*₆₋₅ = 3.2 Hz, 1H, H₆), 3.72 (dd, *J*_{6-6'} = 11.4 Hz, *J*_{6'-5} = 5.3 Hz, 1H, H_{6'}), 2.73 (br, s, 2H, -OH, -OH), 1.48 (s, 3H, -CH₃), 1.31 (s, 3H, -CH₃). MS (EI): 260 (0.3, M⁺), 245 (24.7, M⁺-CH₃), 113 (100).

1,2-*O*-isopropyliden-3-*O*-(2-methyl-2-propenyl)- β -D-glucofuranose (17b). It was prepared (430 mg, 98%) from **16b** (500 mg, 1.59 mmol) and 33% acetic acid (5 mL) according to the procedure described above for **17a**. ¹H-NMR (250 MHz, CDCl₃) δ : 5.93 (d, J =3.8, 1H, H₁), 5.00 (s, br, 1H, H₂C=), 4.93 (s, br, 1H, H₂C=), 4.59 (d, J =3.8, 1H, H₂), 4.2-4.0 (m, 5H, H₃, H₄, H₅, -CH₂O-), 4.0-3.8 (m, 2H, 2H₆), 2.73 (d, J =6.4, 1H, C5-OH), 2.11 (s, br, 1H, C6OH), 1.76 (s, 3H, -CH₃), 1.50 (s, 3H, -CH₃), 1.33 (s, 3H, -CH₃). MS (EI): 274 (1.8, M⁺), 259 (3.2, M⁺-CH₃), 55 (100). HRMS calc. for C₁₃H₂₂O₆: 274.1416; Found: 274.1413.

1,2-*O*-isopropyliden-3-*O*-(2-methyl-1-propenyl)- β -D-glucofuranose (17c). It was prepared (825 mg, quantitative) from **16c** (940 mg, 2.99 mmol) and 33% acetic acid (6 mL) according to the procedure described above for **17a**. ¹H-NMR (250 MHz, CDCl₃) δ : 5.88 (m, 2H, H₁, CH=), 4.52 (d, J =3.7, 1H, H₂), 4.21 (d, J =2.9, 1H, H₃), 4.15 (dd, J =8.3, J =2.9, 1H, H₄), 4.01 (m, 1H, H₅), 3.84 (dd, J =11.6, J =2.9, 1H, H₆), 3.72 (dd, J =11.6, J =5.4, 1H, H₆), 1.55 (s, 3H, -CH₃), 1.54 (s, 3H, -CH₃), 1.47 (s, 3H, -CH₃), 1.29 (s, 3H, -CH₃). ¹³C-NMR (62.9 MHz, CDCl₃) δ : 138.0 (CH=), 113.6 (C=), 112.0 (C(CH₃)₂), 105.1 (C₁), 83.0, 82.4, 79.6 (C₂, C₃, C₄), 68.8 (C₅), 64.2 (C₆), 26.6, 26.2, 19.4, 15.1 (CH₃, CH₃, CH₃, CH₃). MS (EI): 274 (23, M⁺), 259 (3.8, M⁺-CH₃), 58 (100). HRMS calc. for C₁₃H₂₂O₆: 274.1416; Found: 274.1413.

3-*O*-Allyl-6-*O*-(*tert*-butyldimethylsilyl)-1,2-isopropylidene- β -D-glucofuranose (18a).⁵

Imidazole (241 mg, 3.54 mmol) and *tert*-butyldimethylsilyl chloride (534 mg, 3.54 mmol) were added to a solution of **17a** (838 mg, 3.22 mmol) in DMF (12 mL) at 0 °C. After 1 h., the reaction mixture was diluted with water and extracted with diethyl ether. The organic extracts were dried over Na₂SO₄. Purification through silica gel gave **18a** (863 mg, 70%).

6-*O*-(*tert*-Butyldimethylsilyl)-1,2-*O*-isopropylidene-3-*O*-(2-methyl-2-propenyl)- β -D-glucofuranose (18b). It was prepared (460 mg, 90%) from **17b** (360 mg, 1.31 mmol), DMF (5 mL), imidazole (100 mg, 1.50 mmol) and *tert*-butyldimethylsilyl chloride (230 mg, 1.50 mmol) according to

the procedure described for **18a**. ^1H -NMR (300 MHz, CDCl_3) δ : 5.89 (d, $J=3.7$, 1H, H_1), 5.00 (m, 1H, $=\text{CH}_2$), 4.91 (m, 1H, $=\text{CH}_2$), 4.55 (d, $J=3.7$, 1H, H_2), 4.11-3.73 (m, 7H, H_3 , H_4 , H_5 , H_6 , H_6' , CH_2), 2.70 (d, $J=6.5$, 1H, -OH), 1.47 (s, 3H, $-\text{CH}_3$), 1.31 (s, 3H, $-\text{CH}_3$), 0.90 (s, 9H, $-\text{C}(\text{CH}_3)_3$), 0.00 (s, 6H, $-\text{CH}_3$). ^{13}C -NMR (75.47 MHz, CDCl_3) δ : 141.6 (C=), 112.8 ($\text{CH}_2=$), 111.6 ($\text{C}(\text{CH}_3)_2$), 105.1 (C_1), 82.3, 81.5, 79.5 (C_2 , C_3 , C_4), 68.3 (C_5), 64.5 (C_6), 26.7, 26.3 ($\text{C}(\text{CH}_3)_2$), 25.9 ($\text{C}(\text{CH}_3)_3$), 18.3 ($\text{C}(\text{CH}_3)_3$), -5.4 (Si- CH_3). MS (EI): 373 (0.8, M^+-CH_3), 117 (100). MS (FAB $^+$): 389 (M^++1). HRMS (FAB $^+$) calc. for $\text{C}_{19}\text{H}_{37}\text{O}_6\text{Si}$: 389.2359; Found: 389.2363.

6-*O*-benzyl-1,2-*O*-isopropylidene-3-*O*-(2-methyl-1-propenyl)- β -D-glucofuranose (18c**).**

A suspension of **17c** (14 mg, 0.05 mmol) and $n\text{-Bu}_2\text{SnO}$ (14 mg, 0.05 mmol) in dry benzene and molecular sieves 4A was refluxed for 2h. After cooling down to rt, benzyl bromide (6 μL , 0.05 mmol) was added, and the reaction mixture refluxed again. Removal of the solvent and column chromatography (AcOEt-hexane 25-75) gave **18c** as an oil (10 mg, 55%). ^1H -NMR (300 MHz, CDCl_3) δ : 5.89 (d, $J=3.7$, 1H, H_1), 5.00 (m, 1H, $=\text{CH}_2$), 4.91 (m, 1H, $=\text{CH}_2$), 4.55 (d, $J=3.7$, 1H, H_2), 4.11-3.73 (m, 7H, H_3 , H_4 , H_5 , H_6 , H_6' , CH_2), 2.70 (d, $J=6.5$, 1H, -OH), 1.47 (s, 3H, $-\text{CH}_3$), 1.31 (s, 3H, $-\text{CH}_3$), 0.90 (s, 9H, $-\text{C}(\text{CH}_3)_3$), 0.00 (s, 6H, $-\text{CH}_3$). ^{13}C -NMR (75.47 MHz, CDCl_3) δ : 141.6 (C=), 112.8 ($\text{CH}_2=$), 111.6 ($\text{C}(\text{CH}_3)_2$), 105.1 (C_1), 82.3, 81.5, 79.5 (C_2 , C_3 , C_4), 68.3 (C_5), 64.5 (C_6), 26.7, 26.3 ($\text{C}(\text{CH}_3)_2$), 25.9 ($\text{C}(\text{CH}_3)_3$), 18.3 ($\text{C}(\text{CH}_3)_3$), -5.4 (Si- CH_3). MS (EI): 373 (0.8, M^+-CH_3), 117 (100). MS (FAB $^+$): 389 (M^++1). HRMS (FAB $^+$) calc. for $\text{C}_{19}\text{H}_{37}\text{O}_6\text{Si}$: 389.2359; Found: 389.2363.

3-*O*-Allyl-6-*O*-(*tert*-butyldimethylsilyl)-5-oxo-1,2-isopropylidene- β -D-xylo-furanose (4i**).** It was obtained (738 mg, 80%) from **18a** (941 mg, 2.51 mmol), PCC (2167 mg, 10.05 mmol) and molecular sieves (4 Å, 2 g) as reported for **4f**. Total reaction time 2 h. ^1H NMR (CDCl_3 , 300 MHz) δ : 6.02 (d, $J_{1-2} = 3.6$ Hz, 1H, H_1), 5.79 (m, $J_{\text{trans}} = 17.2$ Hz, $J_{\text{cis}} = 10.3$ Hz, $J_{\text{gem}} = 5.6$ Hz, 1H, $-\text{O}-\text{CH}_2-\text{CH}=\text{CH}_2$), 5.26-5.16 (m, 2H, $-\text{O}-\text{CH}_2-\text{CH}=\text{CH}_2$), 4.84 (d, $J_{3-4} = 3.6$ Hz, 1H, H_4), 4.55 (d, $J_{1-2} = 3.6$ Hz, 1H, H_2), 4.54 (d, $J_{6-6'} = 19.0$ Hz, 1H, H_6), 4.46 (d, $J_{6-6'} = 19.0$ Hz, 1H, H_6'), 4.29 (d, $J_{3-4} = 3.6$ Hz, 1H, H_3), 4.04

(dd, $J_{\text{gem}} = 12.8$ Hz, $J = 5.4$ Hz, 1H, -O-CH₂-CH=CH₂), 3.94 (dd, $J_{\text{gem}} = 12.8$ Hz, $J = 5.8$ Hz, 1H, -O-CH₂-CH=CH₂), 1.47 (s, 3H, CH₃), 1.32 (s, 3H, CH₃), 0.92 (s, 9H, t-Bu), 0.08 (s, 3H, Si-CH₃), 0.06 (s, 3H, Si-CH₃). ¹³C NMR (CDCl₃, 75 MHz) δ : 205.1 (C5), 133.5 (CH=CH₂), 118.1 (C(CH₃)₂), 112.3 (CH=CH₂), 105.7 (C1), 84.7, 83.2, 81.9 (C2, C3, C4), 71.3 (C6), 68.9 (-O-CH₂), 26.9, 26.3 ((CH₃)₂C-), 25.8 (CH₃-Si-), 18.4 ((CH₃)₂C-), -5.5, -5.4 (Si-CH₃). IR: 3470 (-OH), 2906 (=CH₂), 1738 (C=O), 1374 (-C(CH₃)₃), 1252, 845. MS m/z (%): 357 (4, (M-CH₃)⁺), 315, 257, 215, 199, 171 (100, (M-TBDMS)⁺), 73 (45, (CH₃)₄C). MS (FAB⁺): 373 (M⁺+1). HRMS (FAB⁺) calc. for C₁₈H₃₃O₆Si: 373.2046; Found: 373.2050.

6-*O*-(*tert*-Butyldimethylsilyl)-1,2-*O*-isopropylidene-3-*O*-(2-methyl-2-propenyl)-5-oxo- β -D-xilofuranose (4j). It was prepared (260 mg, 58%), according to the procedure described for **4f**, from **18b** (450 mg, 1.16 mmol), PCC (1 g, 4.23 mmol),) and molecular sieves (4 Å, 580 mg), and purified by column chromatography (AcOEt-hexane 10-90, 25-75). ¹H-NMR (300 MHz, CDCl₃) δ : 5.96 (d, $J=3.6$, 1H, H₁), 4.91 (m, 2H, =CH₂), 4.85 (d, $J=3.6$, 1H, H₄), 4.56 (d, $J=3.6$, 1H, H₂), 4.52 (s, 1H, H₆), 4.50 (s, 1H, H₆), 4.29 (d, $J=3.6$, 1H, H₃), 3.94 (d, $J=12.3$, 1H, CH₂), 3.85 (d, $J=12.3$, 1H, CH₂), 1.47 (s, 3H, CH₃), 1.33 (s, 3H, CH₃), 0.91 (s, 9H, t-Bu), 0.10 (s, 6H, Si-CH₃). ¹³C-NMR (75.47 MHz, CDCl₃) δ : 205.0 (C₅), 140.8 (C=), 113.3 (CH₂), 112.3 (C(CH₃)₂), 105.6 (C₁), 84.6, 83.2, 81.6 (C₂, C₃, C₄), 74.2 (CH₂), 68.8 (CH₂), 26.9, 26.3 ((CH₃)₂C-), 25.8 (CH₃-Si-), 18.4 ((CH₃)₂C-), -5.4 (Si-CH₃). IR: 2935, 1734 (C=O), 1378, 1077. MS (FAB⁺): 387 (M⁺+1). HRMS (FAB⁺) calc. for C₁₉H₃₃O₆Si: 385.2046; Found: 385.2041.

6-*O*-benzyl-1,2-*O*-isopropylidene-3-*O*-(2-methyl-1-propenyl)-5-oxo- β -D-xilofuranose (4k). It was obtained (125 mg, 70%) from **18c** (180 mg, 0.49 mmol), Dess-Martin periodinane (250 mg, 0.59 mmol) and *tert*-butanol (56 μ L, 0.59 mmol) as reported for **4a** and purified by flash chromatography (AcOEt-hexane 10-90). ¹H-NMR (250 MHz, CDCl₃) δ : 7.36-7.31 (m, 5H, ArH), 6.01 (d, $J=3.5$, 1H, H₁), 5.73 (m, 1H, CH=), 4.81 (d, $J=3.4$, 1H, H₄), 4.58 (s, 1H, CH₂), 4.57 (s, 1H, CH₂), 4.54 (d, $J=3.5$,

1H, H₂), 4.46 (d, *J*=3.4, 1H, H₃), 4.43 (s, 1H, H₆), 4.40 (s, 1H, H₆), 1.51 (d, *J*=0.8, 3H, -CH₃), 148 (s, 3H, CH₃), 1.46 (d, *J*=0.8, 3H, -CH₃), 1.32 (s, 3H, -CH₃). ¹³C-NMR (62.9 MHz, CDCl₃) δ : 203 (C=O), 137.4 (CH=), 137.2 (Ar_{ipso}), 128.4, 127.9 (ArH), 114.3 (C=), 112.6 (C(CH₃)₂), 105.6 (C₁), 84.5, 84.3, 82.0 (C₂, C₃, C₄), 74.3 (CH₂), 73.3 (CH₂), 26.9, 26.3, 19.3, 15.1 (CH₃, CH₃, CH₃, CH₃). IR: 2984, 1733 (C=O), 1378, 1020. MS (FAB⁺): 363 (M⁺+1). HRMS (FAB⁺) calc. for C₂₀H₂₆O₆: 362.1729; Found: 362.1727.

Ketone 4I. Jones' reagent was added dropwise to a solution of 6-*O*-benzyl-3-deoxy-1,2-*O*-diisopropylidene-3-*C*-methyl- α -D-allofuranose⁶ (840 mg, 2.72 mmol) in acetone (1 mL) at rt. The reaction mixture was neutralized with a saturated aqueous solution of NaHCO₃ and the product extracted with CH₂Cl₂. Drying over Na₂SO₄, removal of the solvent and flash chromatography (AcOEt-hexane 15-85) gave **4I** (640 mg, 76%). ¹H-NMR (300 MHz, CDCl₃) δ : 7.28-7.19 (m, 5H, ArH), 5.75 (d, *J*=3.4, 1H, H₁), 4.53 (s, 1H, H₇), 4.52 (s, 1H, H₇), 4.5 (dd, 1H, H₂), 4.35 (s, 1H, H₆), 4.34 (s, 1H, H₆), 4.1 (d, *J*=10.6, 1H, H₄), 1.95 (m, 1H, H₃), 1.41 (s, 3H, CH₃), 1.24 (s, 3H, CH₃), 1.1 (d, *J*=6.8, 1H, CH₃). ¹³C-NMR (75.4 MHz, CDCl₃) δ : 205.9 (C=O), 137.2 (Ar_{ipso}), 128.5, 128.0 (ArH), 112.3 (C(CH₃)₂), 105.5 (C₁), 85.2, 82.3 (C₅, C₄, C₂), 73.2, 72.0 (C₇, C₆), 42.7 (C₃), 26.8, 26.3 (CH₃, CH₃), 9.5 (CH₃). IR: 2925, 1728 (C=O), 1103, 1026. MS (EI): 306 (0.15, M⁺), 291 (1.0, M⁺-CH₃), 157 (41), 91 (100, C₇H₇). HRMS (EI) calc. for C₁₇H₂₁O₅: 305.1389; Found: 305.1383.

Nitrone 5I. MeNHOH.HCl (320 mg, 3.8 mmol) and pyridine (200 μ L, 2.53 mmol) were added to a solution of ketone **4I** (194 mg, 0.63 mmol) in ethanol (5 mL) at rt for 19 h. Removal of the solvent *in vacuo* and filtration through silica gel (MeOH- CH₂Cl₂ 1-99) gave **5I** (134 mg, 63%) and **4I** (41 mg, 21%). ¹H-NMR (250 MHz, CDCl₃) δ : 7.32-7.19 (m, 5H, ArH), 5.68 (d, *J*=3.5, 1H, H₁), 5.43 (d, *J*=10.4, 1H, H₄), 4.46 (s, 2H, H₇, H₇), 4.42 (dd, 1H, H₂), 4.15 (d, *J*=12.3, 1H, H₆), 4.02 (d, *J*=12.3, 1H, H₆), 3.71 (s, 3H, CH₃), 1.90 (m, 1H, H₃), 1.48 (s, 3H, CH₃), 1.26 (s, 3H, CH₃). MS (EI): 291 (2.5), 157

(60.5), 91 (100, C₇H₇). MS (FAB⁺): 337 (5, M⁺⁺²), 336 (M⁺⁺¹), 154 (100). HRMS (FAB⁺) calc. for C₁₈H₂₆NO₅: 336.18109; Found: 336.1812.

¹ For the alternative removal of the isopropylidene group of **7a** with pyridinium p-toluenesulfonate to give **8a**, see: Van Rijsbergen, R.; Anteunis, M. J. O.; De Bruyn, A. *J. Carbohydr. Chem.* **1983**, *2*, 395-404.

² Alonso, R. A.; Burgey, C. S.; Rao, B. V.; Vite, G. D.; Vollerthun, R.; Zottola, M. A.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1993**, *115*, 6666-6672.

³ For an alternative procedure, see Smith, A. B., III; Rivero, R. A.; Hale, K. J.; Vaccaro, H. A. *J. Am. Chem. Soc.* **1991**, *113*, 2092-2112.

⁴ Arnold, T.; Orschel, B.; Reissig, H. U. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1033-1035.

⁵ Das, S. K.; Mallet, J.-M.; Esnault, J.; Driguez, P.-A.; Duchaussoy, P.; Sizun, P.; Herault, J.-P.; Herbert, J.-M.; Petitou, M.; Sinay, P. *Chemistry. A European Journal* **2001**, *7*, 4821-4834.

⁶ a) Chida, N.; Takeoka, J.; Ando, K.; Tsutsumi, N.; Ogawa, S. *Tetrahedron* **1997**, *53*, 16287-16298. b) Oikawa, Y.; Tanaka, T.; Horita, K.; Noda, I.; Nakajima, N.; Kakusawa, N.; Hamada, T.; Yonemitsu, O. *Chem. Pharm. Bulletin* **1987**, *35*, 2184-2195.

7a

8a

9a

36.939

35,421

8b

98

9b

9b

4d

4d

12

12

13

4f

5f

5f

5f

5f

5g

5g

5h

4j

4l

51

19a

19a

19a

19a

19a

19b

19b

19c

19c

19d

19d

COSY

CORREL. C - H

19d'

20

21

21

19f

19f

19f

19f

19f

19g , R = CO₂Me

19h'

19i
(C₆D₆, ta)

19i
(CDCl₃, ta)

19i

(C₆D₆, 323K)

19i

19i

19i

19j

(C6D6, 327K)

19j

19k

19k

19la