A Method for the Syntheses of Enopyranosides

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Abstract: Sodium hydride (NaH) in hexamethylphosphoric triamide (HMPA) has been introduced as an economical and efficient reagent towards the creation of 1,2- or 5,6-enopyranosides from the corresponding halogenated or tosylated pyranosides. NaH/HMPA has several advantages compared to NaH/*DMF*: elimination products are produced in high yields even from sterically-hindered halides as well as tosylates.

Keywords: Enopyranosides, sodium hydride/hexamethylphosphoric triamide, carbohydrates.

Unsaturated sugar derivatives are an important class of chiral building blocks which can be modified into useful synthons, also for the synthesis of chiral natural products. There are various types of unsaturated carbohydrates which can be prepared by insertion of a double bond into the carbohydrate skeleton and may be categorized in three major classes including alkenes, enols and enediols. The unsaturation may be exo- or endocyclic in nature. Syntheses and properties of various unsaturated carbohydrates are reported frequently in the literature [1-3]. Glycals and 2-hydroxyglucals are usually prepared by the elimination of hydrogen bromide from acylglycosyl bromides by treatment with Zn/Cu in acetic acid and its modified version [4] or secondary amines [5], by conversion of the bromides to iodides prior to reaction with the base (diethylamine) [2a] and more recently with the dimeric Ti (III) species $(Cp_2TiCl)_2$ or by using NaH in DMF [6]. A new avenue had been opened up for the application of 6-deoxy-hex-5-enopyranoses when a number of methods were developed for their easy transformation to cyclohexane (cylitols) and cyclopentane skeletons by replacing the ring oxygen atom of the sugar moiety by a methylene group [7,8]. Thus, 6-deoxy-hex-5-enopyranosides become useful starting materials for the synthesis of prostaglandins [8a], accessible by treating of 6-bromo-, 6-iodo-6-deoxyhexopyranosides or 6-*O*-*p*-tosylhexopyranosides with NaH/DMF [6], CsF/DMF [9], AgF/pyridine [10], 1,8-diazabicyclo[5.4.0]undec-7-ene(DBU)/CH_3CN [11], NaI/Bu_4NI/MS 4A/DBU/DMSO [12] or DBU/DMF [13]. However, most of these methods suffer from the formation of undesired by-products or low yields.

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RESULTS AND DISCUSSIONS

Previously, we reported the cleavage of silyl ethers with sodium hydride in HMPA [14] and the selectivity of this reagent towards the cleavage of *tert*-butyldiphenylsilyl ethers in the presence of *tert*-butyldimethylsilyl ethers [15]. In a short communication [16] we reported preliminary results on the synthesis of 2-hydroxyglycals, 1,2-enopyranosides, and 5,6-enopyranoses using sodium hydride (NaH) in HMPA from α-halo or α-tosyloxy sugars neighbored by a β-hydrogen *via* elimination of HX and HOTs, respectively. Due to the wide applicability of the easily accessible enopyranoses and this derivative *via* the NaH/HMPA method we thought it necessary to present here more experimental synthetic details and data for the earlier reported compounds and extend the method to the synthesis of more difficult to approach 3,4-enopyranoses.

In a typical reaction, to a suspension of a 2.2 molar equivalent oil-free NaH, 2.2 mol of a 1 molar halogenated or tosylated starting material in anhydrous HMPA under argon was added dropwise at 0 °C a solution of 1 molar equivalent of halogenated or tosylated starting material in anhydrous HMPA (in cases where the starting material is insoluble in HMPA, a saturated solution of starting material in THF can be added). The mixture was stirred at room temperature for the time given in Table **1**. Upon completion of the reaction (TLC analysis, 12 to 24 h), quenching was performed either with wet diethyl ether or water and the mixture filtered through a pad of Celite. Aqueous work up of the filtrate and silica gel chromatography afforded the pure β-elimination products (Scheme **1**).

According to Table **1** the NaH/HMPA procedure gives higher yields of elimination products from halides as well as tosylates compared to those reported for NaH/DMF [6]. For instance using NaH/DMF for entries 1,7,8,9, less than 5% yield and a complex mixture of non-separable side products were reported [6].

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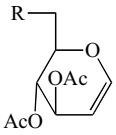
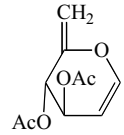
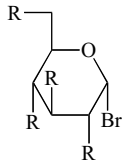
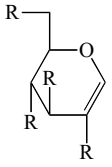
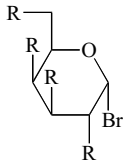
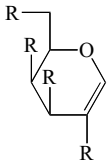
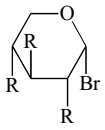
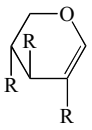
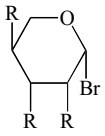
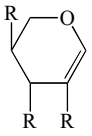
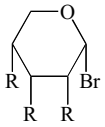
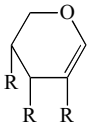
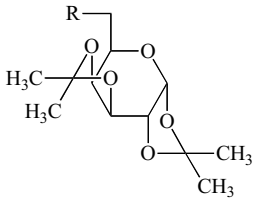
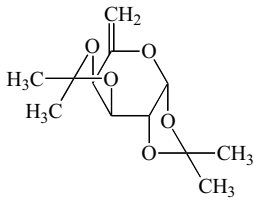
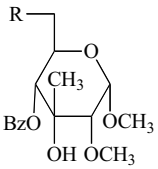
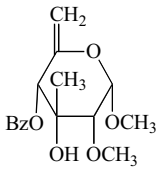
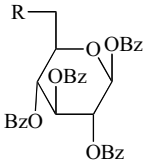
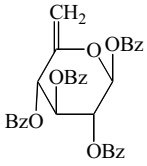
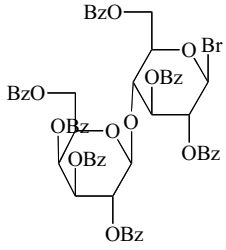
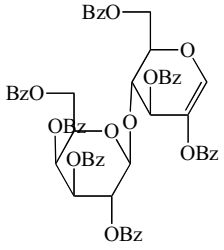
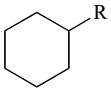
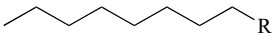
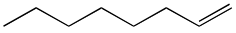
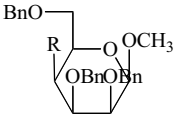
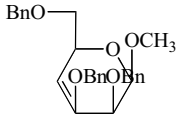
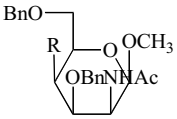
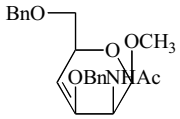
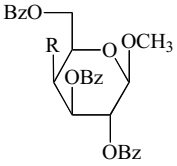
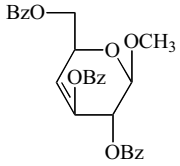
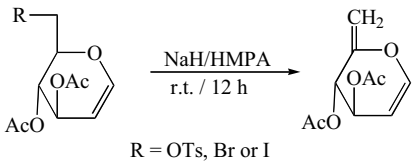
Table 1. NaH in HMPA as HX and HOTs Eliminating Agent

Entry	Starting Material	Product	Reaction Time/h	% Yield (Isolated)
1	 **1** R = OTs, **3** R = Br, 4 R = I	 **2**	12 13 12	90 96 97
2	 **5** R = OAc, **6** R = OBz	 **7** R = OAc, **8** R = OBz	12 12	91 93
3	 **9** R = OAc, **10** R = OBz	 **11** R = OAc, **12** R = OBz	12 12	91 93
4	 **13** R = OAc	 **14** R = OAc	12	89
5	 **15** R = OAc	 **16** R = OAc	18	91
6	 **17** R = OAc	 **18** R = OAc	24	87
7	 **19** R = OTs, **20** R = Br, **21** R = I	 **22**	22	95 90 88
8	 **23** R = OTs, **24** R = Br, **25** R = I	 **26**	17	90 87 85

(Table 1). Contd…..

Entry	Starting Material	Product	Reaction Time/h	% Yield (Isolated)
9	 **27** R = OTs, **28** R = Br, **29** R = I	 **30**	23	92 86 87
10	 **31**	 **32**	16	97
11	 **33** R = OTs, **34** R = I	 **35**	14 12	94 92
12	 **36** R = OTs, **37** R = I	 **38**	13 14	88 87
13	 **39** R = OTs, **40** R = Br, **41** R = I	 **42**	3 3 3	90 88 90
14	 **43** R = OTs, **44** R = Br, **45** R = I	 **46**	3 3 3	90 85 87
15	 **47** R = OTs, **48** R = Br, **49** R = I	 **50**	4 4 4	91 85 86



R = OTs, Br or I

Scheme 1.

In conclusion, NaH in HMPA [16] provides a reagent producing elimination products from halides [17-28] as well as *p*-toluenesulfonic acid esters in high yields. The method is equally suitable for the preparation of 1,2-, 5,6-enopyranosides and otherwise more difficult to synthesize 3,4-enopyranosides. The use of NaH and HMPA is thus probably the most generally applicable reagent to produce unsaturated carbohydrates, compatible with many protecting and functional groups *via* elimination from halo and tosylated carbohydrates.

EXPERIMENTAL

All chemicals and reagents were obtained from commercial suppliers and used as such without further purification. Solvents were dried and distilled according to standard pro-

cedures. The reactions were monitored by thin-layer chromatography, carried out on 0.25 mm silica gel plates (60 F-254, Merck, Darmstadt, Germany). Plates were visualized under UV light (where appropriate), sprayed with an orcinol/H_2SO_4/$FeCl_3$ solution and heated to develop. Column chromatography was performed on silica gel 60 (0.063-0.200 mm, Merck, Darmstadt, Germany), using the indicated solvent system. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ on a Bruker AC 250 (^{1}H NMR: 250 MHz, ^{13}C NMR: 63 MHz) or a Bruker WM 400 spectrometer (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz). The chemical shifts are reported in parts per million (ppm) on a δ scale from *TMS* as internal standard. The EI, FAB and FD mass spectra were recorded on a Finnigan MAT 312 mass spectrometer connected to a PDO 11/34 (DEC) computer system. Optical rotations were obtained with an LEP AZ polarimeter (Zeiss, Jena) at 546 nm. All melting points are uncorrected.

General Procedure for Dehydrohalogenation and Dehydrotosylation

To a suspension of oil-free NaH (2.2 molar equivalent) in anhydrous HMPA (1 ml per mmol) under argon was added at 0 °C dropwise the halogenated or tosylated material (1 molar equivalent) in anhydrous HMPA (1 ml per mmol). The reaction mixture was then allowed to stir at room temperature for a given time period (see Table **1**). After completion of the reaction (TLC analysis), quenching was performed with water and filtered through a bed of Celite. The filtrate was dissolved in appropriate solvent and washed with water to remove HMPA and then with a 1 % aqueous solution of HCl for neutralization. The organic phase was washed with water once again then dried over anhydrous sodium sulfate and concentrated under vacuum. The residue was purified by short column chromatography (silica gel 60, Merck, mesh 0.063-0.200 mm).

3,4-Di-O-acetyl-hex-1,2:5,6-dienopyranoside (2, $C_{10}H_{12}O_5$)

Starting with 0.381, 0.293 or 0.340 g (1 mmol) of **1**, **3** or **4**, after completion of reaction in 12 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **2** was collected as white needles. Yields 0.191 g (90%) [16], 2.04 g (96%) [16] and 0.206 g (97%) [16] from compounds **1**, **3** and **4**, respectively; mp 64-65 °C, $[\alpha]^{25}_D$ = 21 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.65 (dt, $J_{6,6'}$ = 1.6, $J_{6,4}$ = 1.7 Hz, H-6), 4.91 (d, $J_{6',6}$ = 1.6 Hz, H-6'), 5.08 (dd, $J_{2,3}$ = 1.4, $J_{2,1}$ = 5.1 Hz, H-2), 5.10 (dd, $J_{3,2}$ = 1.4, $J_{3,4}$ = 3.1 Hz, H-3), 5.42 (dd, $J_{4,6}$ = 1.7, $J_{4,3}$ = 3.1 Hz, H-4), 6.54 (dd, $J_{1,3}$ = 0.6, $J_{1,2}$ = 5.1 Hz, H-1) ppm; MS-EI: *m/z* (%) = 212 (24) [M^+], 197 (100), 169 (58), 153 (81), 94 (30).

2,3,4,6-Tetra-O-acetyl-2-hydroxy-D-glucal (7, $C_{14}H_{18}O_9$)

Starting with 0.411 g (1 mmol) of **5**, after completion of reaction in 12 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **7** was collected as white needles. Yield 0.3 g (91%) [16]; mp 64-67 °C [16]; $[\alpha]^{25}_D$ = - 21 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.97, 1.98, 2.00, 2.01 (s, $COCH_3$), 4.14 (dd, $J_{6',5}$ = 2.9, $J_{6',6}$ = 11.0 Hz, H-6'), 4.29 (ddd, $J_{5,6'}$ = 2.9, $J_{5,4}$ = 5.3, $J_{5,6}$ = 6.4 Hz, H-5), 4.34 (dd, $J_{6,5}$ = 6.4, $J_{6,6'}$ = 11.0 Hz, H-6), 5.14 (dd, $J_{4,3}$ = 4.4, $J_{4,5}$ = 5.3 Hz, H-4), 5.46 (d, $J_{3,4}$ = 4.4 Hz, H-3), 6.5 (s, H-1) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.2, 20.5, 20.6, 20.7 ($COCH_3$), 60.9 (C-6), 66.2 (C-3), 67.4 (C-4), 74.0 (C-5), 127.3 (C-2), 139.2 (C-1), 169.3, 169.4, 169.9, 170.3 ($COCH_3$) ppm; MS-EI: *m/z* (%) = 330 (43) [M^+], 315 (100), 287 (88), 271(56), 270 (30), 257 (23).

2,3,4,6-Tetra-O-benzoyl-2-hydroxy-D-glucal (8, $C_{39}H_{26}O_9$)

Starting with 0.659 g (1 mmol) of **6**, after completion of reaction in 12 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **8** was collected as white needles. Yield 0.538 g (93%) [16]; mp 121-122 °C [16]; $[\alpha]^{25}_D$ = - 77 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.72 (m, H-6), 4.91 (m, H-5, H-6'), 5.86 (t, $J_{4,3}$ = $J_{4,5}$ = 4.1 Hz, H-4), 6.13 (d, $J_{3,4}$ = 4.1 Hz, H-3), 6.98 (s, H-1), 7.35-8.14 (m, 4Ph) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 61.6 (C-6), 66.6 (C-3), 68.3 (C-4), 73.9 (C-5), 127.5 (C-2), 128.4 (C-1), 128.5, 129.0, 129.1, 129.2, 133.6, (Ph), 165.1, 165.4, 165.5, 166.1 (PhCOO) ppm; MS-EI: *m/z* (%) = 578 (18) [M^+], 501 (98), 473 (68), 457 (77), 443 (56), 442 (43), 336 (13), 215 (27), 80 (90).

2,3,4,6-Tetra-O-acetyl-2-hydroxy-D-galactal (11, $C_{14}H_{18}O_9$)

Starting with 0.412 g (1 mmol) of **9**, after completion of reaction in 12 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **11** was collected as white needles. Yield 0.300 g (91%), mp 110-111 °C [16]; $[\alpha]^{25}_D$ = - 6 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.92, 1.97, 2.00, 2.02 (s, $COCH_3$), 4.16 (dd, $J_{6',5}$ = 5.1, $J_{6',6}$ = 11.3 Hz, H-6'), 4.32 (m, H-5, H-6), 5.41 (dd, $J_{4,5}$ = 2.1, $J_{4,3}$ = 4.8 Hz, H-4), 5.77 (td, $J_{3,1}$ = 1.2, $J_{3,4}$ = 4.8 Hz, H-3), 7.21-7.35 (d, $J_{1,3}$ = 1.2 Hz, H-1) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4, 20.5, 20.6, 20.7 ($COCH_3$), 61.3 (C-3), 63.9 (C-4), 64.0 (C-5), 73.3 (C-6), 138.8 (C-1+C-2), 169.3, 169.8, 169.9, 170.4 ($COCH_3$) ppm; MS-EI: *m/z* (%) = 330 (41) [M^+], 315 (100), 287 (75), 271(43), 270 (60), 257 (28).

2,3,4,6-Tetra-O-benzoyl-2-hydroxy-D-galactal (12, $C_{39}H_{26}O_9$)

Starting with 0.660 g (1 mmol) of **10**, after completion of reaction in 12 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **12** was collected as white needles. Yield 0.614 g (93 %) [16]; mp 63-64 °C [16]; $[\alpha]^{25}_D$ = + 36.2 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.70 (m, H-6), 4.92 (m, H-5, H-6'), 5.87 (t, $J_{4,3}$ = $J_{4,5}$ = 4.1 Hz, H-4), 6.11 (d, $J_{3,4}$ = 4.1 Hz, H-3), 6.99 (s, H-1), 7.32-8.13 (m, 4Ph) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 61.5 (C-6), 66.5 (C-3), 68.3 (C-4), 73.7 (C-5), 127.7 (C-2), 128.3 (C-1), 128.5 128.9, 129.1, 129.2, 133.5 (Ph), 166.1, 165.4, 165.2, 165.1 (PhCOO) ppm; MS-EI: *m/z* (%) = 578 (21) [M^+], 501 (100), 473 (56), 457 (81), 443 (87), 442 (72), 336 (19), 215 (45), 80 (90).

2,3,4,Tri-O-acetyl-2-hydroxy-D-xylal (14, $C_{11}H_{14}O_7$)

Starting with 0.340 g (1 mmol) of **13**, after completion of reaction in 12 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **14** was collected as white needles. Yield 0.303 g (89%) [16]; mp 81-82 °C [16]; $[\alpha]^{25}_D$ = - 272 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.99, 2.01, 2.02 (s, $COCH_3$), 3.88 (dd, $J_{5',4}$ = 1.5, $J_{5',5}$ = 12.5 Hz, H-5'), 4.16 (ddd, $J_{5,3}$ = 1.8, $J_{5,4}$ = 2.4, $J_{5,5'}$ = 12.5 Hz, H-5), 4.89 (dd, $J_{4,3}$ = 1.8, $J_{4,5}$ = 2.4 Hz, H-4), 5.27 (t, $J_{3,4}$ = $J_{3,5}$ = 1.8 Hz, H-3), 6.66 (s, H-1) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.6, 20.8, 20.9 ($COCH_3$), 63.3 (C-3), 64.2 (C-4), 67.3 (C-5), 127.4 (C-2), 141.3 (C-1), 169.9, 169.9,

169.8 ($COCH_3$) ppm; MS-EI: *m/z* (%) = 258 (55) [M^+], 243 (100), 215 (87), 199 (64), 140 (44), 81 (32).

2,3,4,Tri-O-acetyl-2-hydroxy-L-xylal (16, $C_{11}H_{14}O_7$)

Starting with 0.340 g (1 mmol) of **15**, after completion of reaction in 18 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **16** was collected as white needles. Yield 0.309 g (91%) [16]; mp 125-127 °C [16]; $[\alpha]^{25}_D$ = + 282 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.99, 2.01, 2.02 (s, $COCH_3$), 3.89 (dd, $J_{5',4}$ = 1.8, $J_{5',5}$ = 12.5 Hz, H-5'), 4.16 (ddd, $J_{5,3}$ = 1.8, $J_{5,5'}$ = 2.5, $J_{5,4}$ = 3.2 Hz, H-5), 4.89 (dd, $J_{4,3}$ = 1.8, $J_{4,5}$ = 3.2 Hz, H-4), 5.27 (t, $J_{3,4}$ = 1.8 Hz, H-3), 6.67 (s, H-1) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.6, 20.8, 20.9 ($COCH_3$), 63.3 (C-3), 64.2 (C-4), 67.3 (C-5), 127.4 (C-2), 141.3 (C-1), 169.8, 169.9, 169.9 ($COCH_3$) ppm; MS-EI: *m/z* (%) = 258 (46) [M^+], 243 (100), 215 (74), 199 (81), 140 (42), 81 (53).

2,3,4,Tri-O-acetyl-2-hydroxy-L-arabinal (18, $C_{11}H_{14}O_7$)

Starting with 0.340 g (1 mmol) of **17**, after completion of reaction in 24 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **18** was collected as white needles. Yield 0.296 g (87%) [16]; mp 55-57 °C [16]; $[\alpha]^{25}_D$ = + 205 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.99, 2.01, 2.03 (s, $COCH_3$), 3.86 (t, $J_{5,4}$ = $J_{5,5'}$ = 10.4 Hz, H-5), 3.97 (ddd, $J_{5,3}$ = 1.3, $J_{5',4}$ = 4.1, $J_{5',5}$ = 10.4 Hz, H-5'), 5.22 (td, $J_{4,3}$ = $J_{4,5'}$ = 4.1, $J_{4,5}$ = 10.4 Hz, H-4), 5.65 (dd, $J_{3,5}$ = 1.3, $J_{3,4}$ = 4.1 Hz, H-3), 6.61 (s, H-1) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.5, 20.6, 20.8 ($COCH_3$), 62.6 (C-3), 64.4 (C-4), 127.0 (C-2 + C-5), 141.2 (C-1) ppm; MS-EI: *m/z* (%) = 258 (33) [M^+], 243 (100), 215 (81), 199 (67), 140 (59), 81 (46).

6-Deoxy-1,2,3,4-di-O-isopropylidene-L-arabino-hex-5-enopyranoside (22, $C_{12}H_{18}O_5$)

Starting with 0.415, 0.324, 0.371 g (1 mmol) of **19**, **20** or **21**, after completion of reaction in 22 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **22** was collected as white needles. Yields 0.394 g (95%) [16], 0.291 g (90%) [16], 0.326 g (88%) [16] from compounds **19**, **20**, and **21**, respectively; mp 89-90 °C [16]; $[\alpha]^{25}_D$ = - 135 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24, 1.32, 1.44, 1.51, (s, CH_3), 4.25 (d, $J_{4,3}$ = 7.9 Hz, H-4), 4.30 (dd, $J_{2,3}$ = 2.4, $J_{2,1}$ = 5.0 Hz, H-2), 4.59 (dd, $J_{3,2}$ = 2.4, $J_{3,4}$ = 7.9 Hz, H-3), 4.71-4.95 (m, H-6, H-6'), 5.52 (d, $J_{1,2}$ = 5.0 Hz, H-1) ppm; MS-EI: *m/z* (%) = 242 (21) [M^+], 227 (100), 212 (80), 200 (65) , 168 (34).

Methyl 4-O-benzyl-6-deoxy-3-C-methyl-2-O-methyl-α-D-ribo-hex-5-enopyranoside (26, $C_{16}H_{20}O_6$)

Starting with 0.481, 0.390 or 0.437g (1 mmol) of **23**, **24** or **25**, after completion of reaction in 17 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **26** was collected as white needles. Yields 0.277 g (90 %), 0.268 g (87 %), 0.262 g (85 %) from compounds **23**, **24**, and **25**, respectively [16]; mp 113-114 °C [16]; $[\alpha]^{25}_D$ = + 121 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.40 (s, CH_3), 3.34 (d, $J_{2,1}$ = 4.0 Hz, H-2), 3.55 (s, 2 OCH_3), 3.61 (s, OH), 4.80 (dd, $J_{6,4}$ = 2.3, $J_{6,6'}$ = 9.1, Hz, H-6, H-6'), 5.11 (d, $J_{1,2}$ = 4.0 Hz, H-1), 5.45 (d, $J_{4,6}$ = 2.3 Hz, H-4), 7.58-8.20 (m, Ph) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 23.0 (Me), 56.9, 58.9 (2 OMe), 73.9, (C-4), 75.0 (C-3), 81.0 (C-2), 98.4 (C-1), 99.2 (C-6), 150.7 (C-5) ppm; MS-EI: *m/z* (%) = 308 (35) [M^+], 293 (100), 291 (41), 277 (81), 260 (51), 246 (89), 231 (21), 203 (48), 187 (55), 173 (29).

1,2,3,4-Tetra-O-benzoyl-6-deoxy-β-D-xylo-hex-5-enopyranoside (30, $C_{34}H_{26}O_9$)

Starting with 0.751, 0.660 or 0.707 g (1 mmol) of **27**, **28** or **29**, after completion of reaction in 23 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **30** was collected as white needles. Yields 0.691 g (92%), 0.568 g (86%), 0.615 g (87%) from compounds **27**, **28**, and **29**, respectively [16]; mp 131-132 °C [16]; $[\alpha]^{25}_D$ = - 11 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.9-5.1 (m, H-6, H-6'), 5.75 (dd, $J_{2,1}$ = 2.9, $J_{2,3}$ = 4.9 Hz, H-2), 5.91 (t, $J_{3,2}$ = 4.9 Hz, H-3), 6.2 (m, H-4), 6.69 (d, $J_{1,2}$ = 2.9 Hz, H-1), 7.4-8.6 (m, 4Ph) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 73.8 (C-4), 74.8 (C-3), 81.1 (C-2), 98.4 (C-1), 99.2 (C-6), 150.7 (C-5), 126.8-139.9 (Ph), 165.1-165.9 ($PhCO_2$) ppm; MS-EI: *m/z* (%) = 578 (28) [M^+], 501 (100), 473 (49), 457 (78), 443 (67), 442 (80), 336 (25), 215 (49), 80 (93).

2,3,6-Tri-O-benzoyl-4-O-(2,3,4,5-tetra-O-benzoyl-β-D-galactopyranosyl)-1,5-anhydro-D-arabino-hex-1-enitol (32, $C_{61}H_{48}O_{17}$)

Starting with 1.053 g (1 mmol) of **31**, after completion of reaction in 13 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **32** was collected as white needles. Yield 1.02 g (97%) [16]; mp 93-94 °C [16]; $[\alpha]^{25}_D$ = + 47 ($CHCl_3$, c = 1) [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.11-4.56 (m, H-4, H-5, H-6, H-6'), 5.10 (d, $J_{1',2'}$ = 7.8 Hz, H-1'), 5.48 (dd, $J_{3',4'}$ = 3.4, 10.4 Hz, H-3'), 5.76 (dd, $J_{2',1'}$ = 7.8, $J_{2',3'}$ = 10.4 Hz, H-2'), 5.82 (d, $J_{4',3'}$ = 3.4 Hz, H-4), 6.23 (d, $J_{3,4}$ = 4.5 Hz, H-3), 6.75 (d, $J_{1,3}$ = 0.6 Hz, H-1), 7.07-7.99 (m, 7Ph) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 61.4 (C-6), 61.8 (C-6'), 67.9 (C-3), 68.8 (C-4), 69.9 (C-5), 71.7 (C-4'), 71.9 (C-5'), 74.9 (C-3'), 75.4 (C-2'), 101.9 (C-1'), 127.2 (C-2), 139.9 (C-1), 127.1-139.9 (Ph), 165.1, 165.2, 165.5, 165.7 ($PhCO_2$) ppm; MS-EI: *m/z* (%) = 1053 (32) [M^+], 976 (100), 948 (59), 932 (71), 918 (24), 783 (67).

1,2-Cyclohexene (35, C_6H_{10})

Starting with 0.254, 0.210 g (1 mmol) of **33** and **34** after completion of reaction in 14 and 12 h (TLC analysis), respectively, and distillation of reaction mixture afforded pure **35** as colorless liquid. Yield 0.0771 g (94%) [16], Liquid [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26-1.28 (m, 4 CH_2), 5.26 (dd, $J_{1,2}$ = $J_{2,1}$ = 6.2, $J_{1,6}$ = $J_{2,3}$ = 4.5 Hz, H-1, H-2) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 29.4-30.7 (C-3, C-4, C-5, C-6), 96.7 (C-1), 97.3 (C-2) ppm; MS-EI: *m/z* (%) = 82 (100) [M^+], 68 (51).

1-Octene (38, C_8H_{16})

Starting with 0.284, 0.240 g (1 mmol) of **36** and **37** after completion of reaction in 13 and 14 h (TLC analysis), respectively, distillation of reaction mixture afforded **38** as colorless liquid. Yields 0.099 g (88%), 0.097 g (87%) from compounds **36** and **37**, respectively [16]; Liquid [16]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.86 (t, $J_{8,7}$ = 6.5 Hz, CH_3), 1.25-1.28 (m, 5 CH_2), 5.62 (dd, $J_{2,1}$ = 6.5, $J_{2,3}$ = 4.5 Hz, H-2), 5.81 (dd, $J_{1,2}$ = $J_{1',2}$ = 6.5, $J_{1,1'}$ = 9.4 Hz, H-1, H-1') ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 23.1 (C-8), 28.6-30.5 (C-3 + C-4 + C-5 + C-6 + C-7), 98.2 (C-2), 98.5 (C-1) ppm; MS-EI: *m/z* (%) = 112 (87) [M^+], 97 (100), 85 (44), 83 (88), 69 (56).

Methyl 2,3,6-tri-O-benzoyl -4-deoxy-β-D-threo-hex-3-enopyranosides (42, $C_{28}H_{24}O_8$)

Starting with 0.661, 0.570, 0.617 g (1 mmol) of **39**, **40**, **41** after completion of reaction in 3 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **42** was collected as liquid. Yields 0.595 g (90%), 0.502 g (88%), 0.595 g (90%) from compounds **39**, **40**, and **41**, respectively; Liquid, $[\alpha]^{25}_D$ = - 1.4 ($CHCl_3$, c = 1.1), (lit. - 1.6) ($CHCl_3$, c = 1.1) [29]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.34 (d, $J_{2,1}$ = 2.0 Hz, H-2), 3.54 (dd, $J_{6,5}$ = 5.6, $J_{6,6'}$ = 9.5 Hz, H-6), 3.57 (s, OCH_3), 3.70 (dd, $J_{6',5}$ = 6.1, $J_{6',6}$ = 9.5 Hz, H-6'), 4.11 (dd, $J_{5,4}$ = 1.6, $J_{5,6}$ = 5.6 Hz, H-5), 4.51 (d, $J_{1,2}$ = 2.0 Hz, H-1), 4.91 (d, $J_{4,5}$ = 1.6 Hz, H-4) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 59.1 (OCH_3), 61.5 (C-6), 66.6 (C-2), 73.9 (C-5), 98.3 (C-4), 101.4 (C-1), 128.5, 128.8, 129.0, 129.1, 133.4, (Ph), 152.3 (C-3), 165.3, 165.4, 166.1 (PhCOO) ppm; MS-EI: *m/z* (%) = 488 (47) [M^+], 473 (51), 457 (74), 411 (100), 383 (66), 367 (89), 246 (55).

Methyl 3,6-di-O-benzoyl-2-acetamido-2,4-dideoxy-β-D-threo-hex-3-enopyranosides (46, $C_{23}H_{23}O_7N$)

Starting with 0.598, 0.507, 0.554 g (1 mmol) of **43**, **44**, **45** after completion of reaction in 3 h (TLC analysis) and column chromatography (ethyl acetate/hexane) pure **46** was collected as liquid. Yields 0.538 g (90%), 0.431 g (85%), 0.482 g (87%) from compounds **43**, **44**, and **45**, respectively; Liquid, $[\alpha]^{25}_D$ = + 2.0 ($CHCl_3$, c = 1.1), (lit. + 2.1) ($CHCl_3$, c = 1.1) [29]; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.01 (s, $COCH_3$), 2.91 (d, $J_{2,1}$ = 1.8 Hz, H-2), 3.01 (s, NH), 3.51 (dd, $J_{6,5}$ = 5.1, $J_{6,6'}$ = 9.8 Hz, H-6), 3.58 (s, OCH_3), 3.60 (dd, $J_{6',5}$ = 6.0, $J_{6',6}$ = 9.8 Hz, H-6'), 3.89 (dd, $J_{5,4}$ = 1.8, $J_{5,6'}$ = 6.0 Hz, H-5), 4.59 (d, $J_{1,2}$ = 1.8 Hz, H-1), 4.88 (d, $J_{4,5}$ = 1.8 Hz, H-4) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 61.6 (C-6), 56.4 (C-2), 73.9 (C-5), 97.3 (C-4), 100.4 (C-1), 128.4, 129.2, 129.3, 129.3, 133.7, (Ph), 152.5 (C-3), 165.1, 166.1 (PhCOO) ppm; MS-EI: *m/z* (%) = 425 (32) [M^+], 410 (69), 394 (51), 382 (78), 367 (38), 348 (41), 336 (28), 320 (49), 304 (100), 290 (17).

Methyl 2,3,6-tri-O-benzoyl-4-deoxy-β-D-threo-hex-3-enopyranosides (50, $C_{28}H_{24}O_8$)

Starting with 0.661, 0.570, 0.617 g (1 mmol) of **47**, **48**, **49** after a reaction time of 4 h and column chromatography (ethyl acetate/hexane) pure **50** was collected as liquid. Yields 0.602 g (91%), 0.485 g (85%), 0.490 g (86%) from compounds **47**, **48**, and **49** respectively; Liquid, $[\alpha]^{25}_D$ = + 2.6 ($CHCl_3$, c = 1); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.24 (d, $J_{2,1}$ = 3.5 Hz, H-2), 3.43 (dd, $J_{6,5}$ = 6.1, $J_{6,6'}$ = 9.5 Hz, H-6), 3.55 (s, OCH_3), 3.62 (dd, $J_{6',5}$ = 6.6, $J_{6',6}$ = 9.5 Hz, H-6'), 4.11 (dd, $J_{5,4}$ = 2.4, $J_{5,6}$ = 6.1 Hz, H-5), 4.75 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.91 (d, $J_{4,5}$ = 2.4 Hz, H-4) ppm; ^{13}C NMR (63 MHz, $CDCl_3$): δ = 59.2 (OCH_3), 61.7 (C-6), 66.4 (C-2), 73.7 (C-5), 96.7 (C-4), 102.2 (C-1), 128.3, 128.6, 129.1, 129.0, 133.2 (Ph), 151.3 (C-3), 165.1, 165.2, 166.3 (PhCOO) ppm; MS-EI: *m/z* (%) = 488 (36) [M^+], 473 (43), 457 (84), 411 (100), 383 (57), 367 (71), 246 (42).

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REFERENCES

[1] a) Ferrier, R.J. *Adv. Carbohydr. Chem.,* **1965**, *20*, 67; b) Hanessian, S. *Adv. Carbohydr. Chem.,* **1966**, *21*,143; c) Butterworth, R.F.; Hanessian, S. *Adv. Carbohydr. Chem.,* **1971**, *26*, 279; d) Blair, M.G. *Adv. Carbohydr. Chem.,* **1954**, *9*, 279; e) Ferrier, R.J. The *Carbohydrates, Chemistry and Biochemistry,* 2nd ed., Academic Press, New York, **1980**; vol. 1B, pp. 843.

[2] a) Ferrier, R.J.; Sankey, G.H. *J. Chem. Soc., (C),* **1966**, 2339; b) Ferrier, R.J.; Sankey, G.H. *J. Chem. Soc., (C),* **1966**, 2345; c) Bock, K.; Pedersen, C. *Acta Chem. Scand.,* **1970**, *24*, 2465.

[3] a) Lichtenthaler, F.W.; El Ashry, E.S.H.; Göckel, V.H. *Tetrahedron Lett.,* **1980**, *21*, 1429; b) Lichtenthaler, F.W.; Jarglis, P. *Tetrahedron Lett.,* **1980**, *21*, 1425; c) Lichtenthaler, F.W.; Kaji, E.; Weprek, S. *J. Org. Chem.*, **1985**, *50*, 3505; d) Lichtenthaler, F.W.; Jarglis, P. *Chem. Ber.,* **1980**, *113*, 489; e) Lichtenthaler, F.W.; Sakakibara, T.; Egert, E. *Chem. Ber.*, **1980**, *113*, 471.

[4] a) Forbes, C.L.; Franck, R.W. *J. Org. Chem.,* **1999**, *64*, 1424; b) Blair, M.G. *Methods Carbohydr. Chem*., **1963**, *2*, 411; c) Fletcher, Jr.; H.G.; Hudson, C.S. *J. Am. Chem. Soc*., **1947**, *69*, 921; d) Major, R.T.; Cook, E.W. *J. Am. Chem. Soc*., **1936**, *58*, 2333.

[5] Lemieux, R.U.; Lineback, D.R. *Can. J. Chem.,* **1965**, *43*, 94.

[6] a) Cavallaro, C.L.; Schwartz, J. *J. Org. Chem.,* **1995**, *60*, 7055; b) Chrètien, F. *Synth. Commun*., **1989**, *19*, 1015.

[7] a) Ferrier, R.J.; Middleton, S. *Chem. Rev*., **1993**, *93*, 2779 and references quoted therein; b) Sollogoub, M.; Mallet, J.-M.; Sinaÿ, P. *Tetrahedron Lett*., **1998**, *39*, 3471.

[8] a) Ferrier, R.J.; Prasit, P. *J. Chem. Soc. Chem. Commun*., **1981**, 983; b) Farr, R.A.; Peet, N.P.; Kang, M.S. *Tetrahedron Lett*., **1990**, *31*, 7109; c) Ferrier, R.J.; Furneaux, R.H.; Prasit, P.; Tyler, P.C.; Brown, K.L.; Gainsford, G.J.; Diehl, J.W. *J. Chem. Soc. Perkin Trans I,* **1983**, 1621; d) Bernet, B.; Vasella, A. *Helv. Chim. Acta,* **1979**, *62*, 2400; e) Bernet, B.; Vasella, A. *Helv. Chim. Acta,* **1979**, *62*, 2411.

[9] Blackburne, I.D.; Frederick, P.M.; Guthrie, R.D. *Aus. J. Chem.,* **1976**, *29*, 381.

[10] Blair, M.G. *Methods Carbohydr*., **1963**, *2*, 415.

[11] Gallagher, T.F.; Horton, D. *Carbohydr. Res.,* **1983**, *116*, 227.

[12] Sato, K.-I.; Kubo, N.; Takada, R.; Aqeel, A.; Hashimoto, H.; Yoshimura, J. *Chem. Lett*., **1988**, 1703.

[13] Adam, S. *Tetrahedron Lett.,* **1988**, *29*, 6589.

[14] Shekhani, M.S.; Khan, K.M.; Mahmood, K. *Tetrahedron Lett.,* **1988**, *29*, 6161.

[15] Shekhani, M.S.; Khan, K.M.; Mahmood, K.; Shah, P.M.; Malik, S. *Tetrahedron Lett.,* **1990**, *31*, 1669.

[16] Khan, K.M.; Perveen, S.; Shah, S.T.A.; Shekhani, M.S.; Voelter, W. *New J. Chem*., **2001**, *25*, 896.

[17] Blattner, R.; Ferrier, R.J. *J. Chem. Soc. Perkin Trans 1,* **1980**, 1523.

[18] Tsvetkov, Y.E.; Byramova, N.E.; Backinowsky, L.V. *Carbohydr. Res.,* **1983**, *115*, 254.

[19] Jain, S.; Suryawanshi, S.N.; Misra, S.; Bhakuni, D.S. *Indian J. Chem. Sect. B,* **1988**, *27*, 866.

[20] Loganathan, D.; Trivedi, G.K. *Carbohydr. Res.,* **1987**, *162*, 117.

[21] a) Varela, O.; De Fina, G.M.; De Lederkremer, R.M. *Carbohydr. Res.,* **1987**, *167*, 187; b) Paulsen, H.; Thiem, J. *Chem. Ber.,* **1973**, *106*, 132.

[22] Kovác, P.; Taylor, R.B. *Carbohydr. Res.,* **1987**, *167*, 153.

[23] Kaji, E.; Osa, Y.; Takahashi, K.; Zen, S. *Chem. Pharm. Bull.,* **1996**, *44*, 15.

[24] S-García, F.; L-Herrera, F.J.; González, M.S.P. *Tetrahedron*, **1995**, *51*, 5491.

[25] Barata, L.E.S.; Marasaioli, A.J.; Valente, L.; Olesker, A.; Lukacs, G.; Thang, T.T. *Carbohydr. Res.,* **1981**, *90*, 326.

[26] Blattner, R.; Ferrier, R.J.; Tyler, P.C. *J. Chem. Soc. Perkin Trans 1*, **1980**, 1535.

[27] Ishikawa, N.; Kitazume, T.; Yamazaki, T.; Mochida, Y.; Tatsuno, T. *Chem. Lett*., **1981**, 761.

[28] Brunet, J.-J.; Gallois, P.; Caubere, P. *J. Org. Chem.,* **1980**, *45*, 1937.

[29] Attolino, E.; Catelani. G.; D'Andrea, F. *Tetrahedron Lett.*, **2002**, *43*, 1685.