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Application of the Reaction of D-Glucose with Meldrum's Acid: Total Synthesis of the Styryl Lactones (+)-Goniofufurone and (+)-7-epi-Goniofufurone

Rainer Bruns, Angelika Wernicke and Peter Köll *

University of Oldenburg, Department of Chemistry,
Organic Chemistry Laboratory,
PO Box 2503, D-26111 Oldenburg, Germany

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Abstract: The syntheses of the styryl lactones (+)-goniofufurone (**1**) and (+)-7-epi-goniofufurone (**2**) from D-glucose are presented. The key steps are the formation of the lactone moiety by reaction of the hemiacetals **15** and **16** with meldrum's acid (**3**) and the addition of phenylmagnesium bromide to the aldehydes **9** or **12**. In the last case, we obtained the L-ido and D-gluco configurated products **13** and **14** in a 3:1 mixture. However, addition of $ZnCl_2$ shifted the diastereomeric ratio towards the desired compound **14**.

Keywords: Acetogenins; Meldrum's acid; Lactones; Carbohydrates;

Introduction

Extracts and leaves of *Goniothalamus* have traditionally been used for the treatment of edema and rheumatism[1], as a pain killer and mosquito repellent[2], and also as an abortifacient[3]. Recently, McLaughlin's group discovered a number of novel styryl lactones from the ethanolic extract of the stem bark of *Goniothalamus giganteus* Hook f. Thomas (Annonaceae). Among the key compounds in this extract were (+)-goniofufurone (**1**)[4] and (+)-7-epi-goniofufurone (**2**)[5]. These styryl lactones show moderate to significant cytotoxicities against several human tumour cell lines. The structure and relative configuration of **1** and **2** were deduced by McLaughlin *et al.* by NMR spectroscopy and X-ray structure analysis, while the absolute configuration was independently established by Shing *et al.*[6] and Jäger's group[7] by synthesis the unnatural enantiomers (-)-**1** and (-)-**2**. Their unique and intriguing structures as well as their antitumour activities have prompted comprehensive efforts in the synthesis of these substances[8]. However, the formation of the lactone function usually remained the most problematic step during these total syntheses approaches.

* e-mail: koell@uni-oldenburg.de

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Recently, we studied the reaction of meldrum's acid with *aldo*-pentoses and *aldo*-hexoses providing a facile way to C-glycosidic-1,4-lactones[9]. Herein, we report on the application of this reaction in an effective synthesis of (+)-goniofufurone (**1**) and 7-epi-goniofufurone (**2**).

Results and Discussion

The reaction of D-glucose with meldrum's acid (**3**) leads to 3,6-anhydro-2-deoxy-D-glycero-D-ido-octono-1,4-lactone (**4**)[9], which is structurally very similar to the styryl lactones **1** and **2**, as depicted in figure 1 and scheme 1.

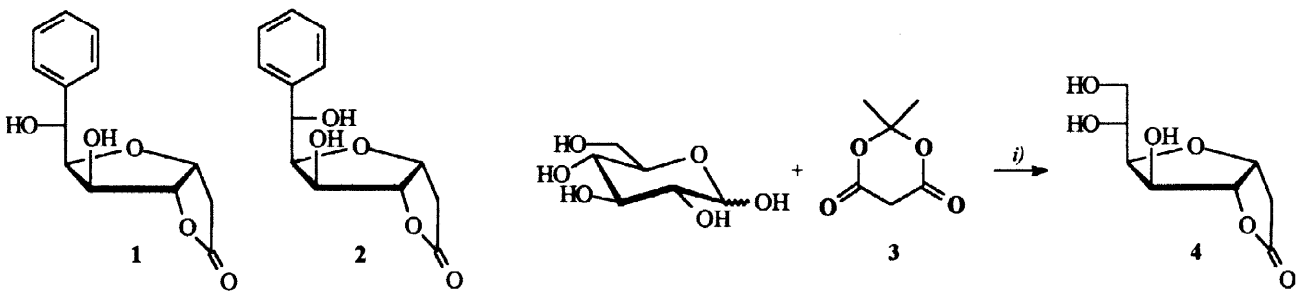
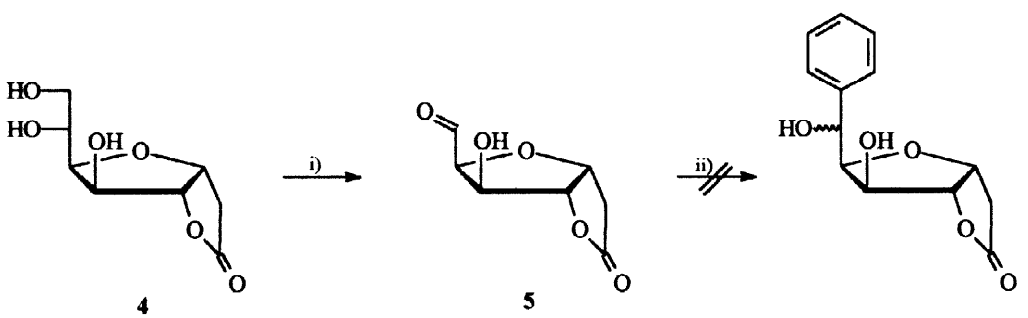


Figure 1: Goniofufurone (1), 7-epi-goniofufurone (2). **Scheme 1:** *Reagents: i) tert.*-butylamine, DMF, 40 °C, 5 d, 90

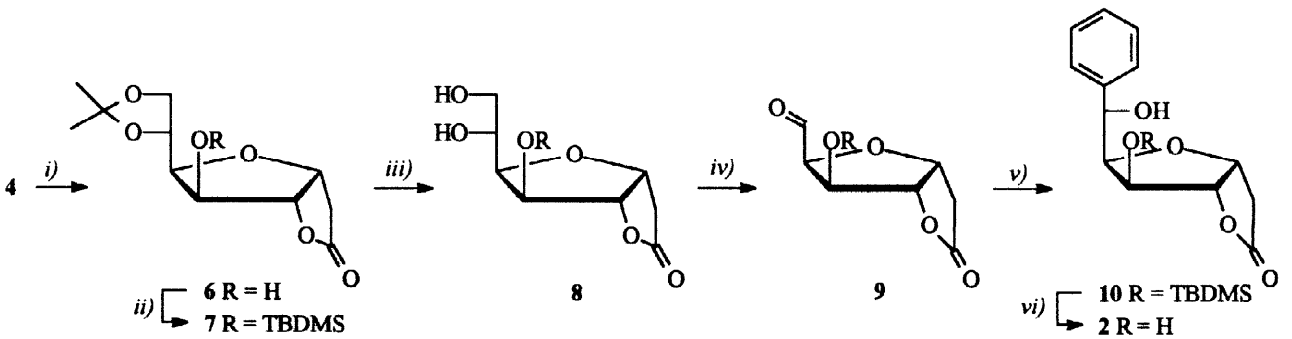
Our initial synthetic strategy is outlined in scheme 2. Periodate cleavage of the vicinal diol function of compound **4** yielded the aldehyde **5**. However, we were not able to find suitable reaction conditions for the addition of phenylmagnesium bromide to the aldehyde. All attempts always lead to complex reaction mixtures.



Scheme 2: *Reagents: i)* $NaIO_4$, $McOH/H_2O$; *ii)* PhMgBr, THF.

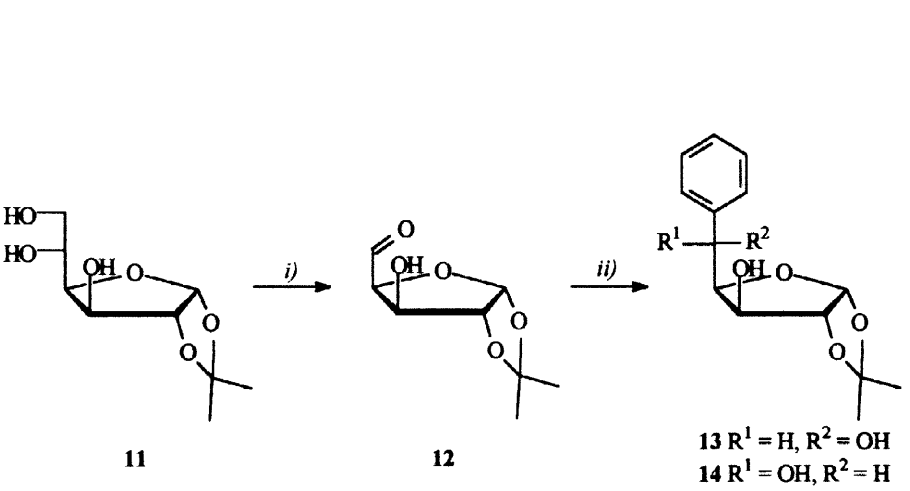
As an enlargement of the synthetic plan we protected the hydroxyl group of **5** as shown in scheme 3. After protection of the vicinal diol as acetal a silylation of the remaining hydroxyl group using TBDMSCl and imidazole in dry DMF gave the derivative **7**. Removal of the acetal using montmorillonite K-10 in methanol performed well. Periodate cleavage of diol **8** released the aldehyde **9** which was subjected to the addition of the phenyl Grignard reagent at low temperature in dry THF giving **10** in moderate yield. Coordination of the

aldehyde and furanoid ring oxygen by the magnesium ion lead to a preferred attack of the nucleophile from the *si*-side giving only the L-glycero-D-ido configurated diastereomer **10** as the main product among with several by-products due to phenylation of the lactone ring, but not the corresponding D-glycero-D-ido diastereomer. Final removal of the silyl ether using the AcCl/MeOH methodology introduced by Hoye[10] furnished the target compound **2** in good yields. All spectroscopic data obtained for **2** are in full agreement with the one published for the material isolated from natural sources.



Scheme 3: *Reagents: i)* acetone, cat. H_2SO_4, rt, 16 h, 79 %; *ii)* TBDMSCl, ImH, DMF, 60 °C, 16 h, 95 %; *iii)* MeOH/H_2O, Montmorillonite K-10, 60 °C, 93 %; *iv)* MeOH/H_2O, $NaIO_4$, 0 °C, 45 min, 93 %; *v)* PhMgBr, THF, -20 °C, 1.5 h, 55 %; *vi)* AcCl/MeOH/THF, rt, 12 h, 60 %.

In order to obtain both diastereomers in the Grignard reaction we changed our strategy and carried out the formation of the lactone moiety as the final step, as it is shown in scheme 4. Following Jäger's procedure[7b]



Scheme 4: *Reagents: i)* $NaIO_4$, MeOH/H_2O, 4 °C, 2 d; *ii)* PhMgBr, THF, $ZnCl_2$, 0 °C, 5 h, rt, 16 h, 62 % (**13**:**14** =1:1).

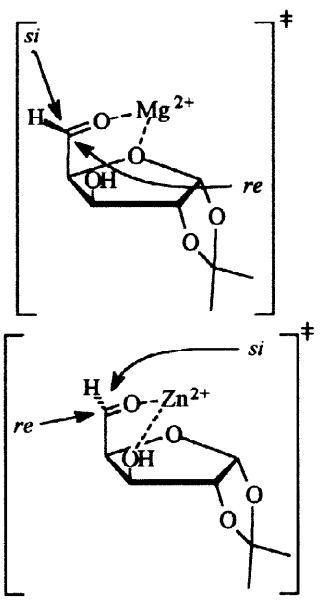
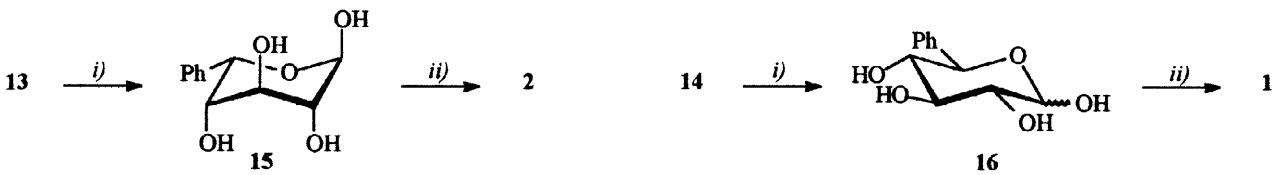


Figure 2

monoacetone D-glucose (**11**)[11] was subjected to a periodate cleavage giving the crude aldehyde **12**. **12** was treated with an excess of phenylmagnesium bromide in dry THF to afford the L-ido and D-gluco configurated products **13** and **14** in a 3 to 1 ratio, which were separated by column chromatography. Since only the minor diastereomer has the correct configuration for a synthesis of **1**, we were looking for a way to shift the diastereomeric ratio towards **14**. This was finally found in the addition of one equivalent $ZnCl_2$ followed by the addition of the Grignard reagent to give **13** and **14** as a 1 to 1 mixture. We assume that the zinc ion coordinates the aldehyde oxygen and the OH group at C-3, thus allows the attack of the nucleophile from the *re*-side as shown in figure 2, while co-ordination by the magnesium ion leads to a preferred attack from the *si*-side.



Scheme 5: *Reagents: i)* HOAc/H_2O (1:1), 80 °C, 25 h, 97 %; *ii)* **3**, $(CH_3)_3CNH_2$, DMF, 40 °C, 5 d, 90 %.

Scheme 5 shows the completion of the reaction sequence. Cleavage of the acetonide function of **13** and **14** using half concentrated acetic acid lead to **15** and **16**, respectively. Conversion of **15** and **16** with meldrum's acid and *tert.*-butylamine in DMF for 5 days gave the target compounds **1** and **2** in good yields. The spectroscopy data for both compounds are again in agreement with the natural material.

In summary, we were able to present a facile route to goniofufurone as well as its 7-epimer. Both were prepared from monoacetone D-glucose in 4 steps in 27 % overall yield.

Acknowledgments: We thank Mrs. M. Rundshagen, Mrs. M. Ehmen, Mr. D. Neemeyer, and Mr. K.-H. Plate for performing the analytical work. R.B. is grateful to the Heinz-Neumüller Foundation for a doctoral fellowship.

Experimental Section

General Methods: All solvents were purified and dried by standard procedures. NMR spectroscopy data were recorded on a Bruker AMX 500 or Bruker AM 300 spectrometer. Chemical shifts are given in the δ-scale in ppm relative to residual nondeuterated solvent signals as internal standard. The coupling constants are reported in Hertz. Optical rotations were determined with a Perkin Elmer 343 polarimeter. Column chromatography was performed on silica gel 60 from Merck. Mass spectra were taken on a Finnigan MAT 212 with data system SS 300 or on a Finnigan MAT 95 with data system DEC-Station 5000 using chemical ionisation with *iso*-butane as

reactant gas. Melting points were determined using a hot-stage microscope SM-Lux from Leitz and are not corrected. Microanalyses were carried out on a Fison Instruments EA 1108.

3,6-Anhydro-2-deoxy-7,8-*O*-isopropylidene-D-glycero-D-ido-octono-1,4-lactone (6): 5.0 g **4** (24.49 mmol) were suspended in dry acetone (100 ml) and a few drops of concentrated H_2SO_4 were added. After stirring overnight at room temperature, the solution was neutralized with saturated aqueous Na_2CO_3. The acetone was removed under reduced pressure and the remaining residue was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. Recrystallization of the residue from CH_2Cl_2/*n*-hexane gave 4.73 g **6** (19.35 mmol, 79 %). R_f = 0.66 (ethyl acetate); $[\alpha]_D^{21}$ = 38.1 (c = 1.08, acetone); mp = 127-128 °C (CH_2Cl_2/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.633 (d, 1 H, $^2J_{2',2}$ = 18.5, $^3J_{2',3}$ = 0, H-2′), 2.718 (dd, 1 H, $^2J_{2',2}$ = 18.5, $^3J_{2,3}$ = 5.7, H-2), 4.963 (dd, 1 H, $^3J_{2',3}$ = 0, $^3J_{2,3}$ = 5.7, $^3J_{3,4}$ = 4.5, H-3), 4.872 (d, 1 H, $^3J_{3,4}$ = 4.5, $^3J_{4,5}$ = 0, H-4), 4.536 (d, 1 H, $^3J_{4,5}$= 0, $^3J_{5,6}$ = 2.5, H-5), 3.930 (dd, 1 H, $^3J_{5,6}$ = 2.5, $^3J_{6,7}$ = 7.7, H-6), 4.283 (ddd, 1 H, $^3J_{6,7}$ = 7.7, $^3J_{7,8'}$ = 5.0, $^3J_{7,8}$ = 5.7, H-7), 3.933 (dd, 1 H, $^2J_{8',8}$ = 8.9, $^3J_{7,8'}$ = 5.0, H-8′), 4.122 (dd, 1 H, $^2J_{8',8}$ = 8.9, $^3J_{7,8}$ = 5.7, H-8), 1.333, 1.401 (s, 3 H, $C(CH_3)_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 175.27 (C-1), 36.11 (C-2), 77.40 (C-3), 87.61 (C-4), 74.34 (C-5), 81.81 (C-6), 73.25 (C-7), 67.43 (C-8), 25.12, 26.73 ($C(\underline{C}H_3)_2$), 109.73 ($\underline{C}(CH_3)_2$); MS: m/z (%) 245 (100) [MH^+]; $C_{11}H_{16}O_6$ (244.24): calc. C 54.08, H 6.61, found C 53.23, H 6.85.

3,6-Anhydro-5-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-7,8-*O*-isopropylidene-D-glycero-D-ido-octono-1,4-lactone (7): 5.0 g **6** (20.47 mmol) and 5.57 g imidazole (81.89) were dissolved in 150 ml dry DMF and stirred together with 4.63 g TBDMSCl (30.71 mmol) at 60 °C for 16 h. After cooling to room temperature, 50 ml water were added to the solution, which was then extracted with *n*-hexane. The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent and crystallization from CH_2Cl_2/*n*-hexane gave 6.89 g **7** (19.47 mmol, 95 %). R_f = 0.70 (ethyl acetate/petroleum ether 1:3); $[\alpha]_D^{21}$ = 26.2 (c = 4.97, acetone); mp = 74 °C (CH_2Cl_2/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.608 (d, 1 H, $^2J_{2',2}$ = 18.4, $^3J_{2',3}$ = 0, H-2′), 2.666 (dd, 1 H, $^2J_{2',2}$ = 18.4, $^3J_{2,3}$ = 5.1, H-2), 4.872 (dd, 1 H, $^3J_{2',3}$ = 0, $^3J_{2,3}$ = 5.1, $^3J_{3,4}$ = 3.8, H-3), 4.681 (d, 1 H, $^3J_{3,4}$ = 3.8, $^3J_{4,5}$ = 0, H-4), 4.430 (d, 1 H, $^3J_{4,5}$= 0, $^3J_{5,6}$ = 2.5, H-5), 3.862 (dd, 1 H, $^3J_{5,6}$ = 2.5, $^3J_{6,7}$ = 7.6, H-6), 4.172 (ddd, 1 H, $^3J_{6,7}$ = 7.6, $^3J_{7,8'}$ = 5.7, $^3J_{7,8}$ = 6.4, H-7), 3.877 (dd, 1 H, $^2J_{8',8}$ = 8.3, $^3J_{7,8'}$ = 5.7, H-8′), 4.050 (dd, 1 H, $^2J_{8',8}$ = 8.3, $^3J_{7,8}$ = 6.4, H-8), 1.289, 1.353 (s, 3 H, $C(CH_3)_2$), 0.120, 0.125 (s, 3 H, $Si(CH_3)_2$), 0.866 (s, 9 H, $SiC(CH_3)_3$); ^{13}C NMR (125.5 MHz, $CDCl_3$): δ = 175.11 (C-1), 36.05 (C-2), 77.10 (C-3), 87.76 (C-4), 74.61 (C-5), 82.70 (C-6), 72.19 (C-7), 67.34 (C-8), 25.18, 26.60 ($C(\underline{C}H_3)_2$), 108.99 ($\underline{C}(CH_3)_2$), -5.29, -5.17 ($Si(\underline{C}H_3)_2$), 25.56 ($SiC(\underline{C}H_3)_3$), 17.97 ($Si\underline{C}(CH_3)_3$); MS: m/z (%) 359 (14) [MH^+], 301 (100) [MH^+-acetone]; $C_{17}H_{30}O_6Si$ (358.50): calc. C 56.95, H 8.44, found C 56.49, H 8.48.

3,6-Anhydro-5-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-glycero-D-ido-octono-1,4-lactone (8): 6.97 g Montmorillonite K-10, which had been activated at 60 °C in a drying oven for several hours, were added to a solution of 5.0 g **7** (13.95 mmol) in MeOH (175 ml) and 35 ml H_2O and stirred at 60 °C until tlc of the reaction mixture indicated the beginning of desilylation. The reaction mixture was rapidly cooled to room temperature and filtrated. The solvent was removed to a final volume of 40 ml and the remaining educt **7** was extracted with *n*-hexane followed by extraction of the product **8** with CH_2Cl_2. Drying over Na_2SO_4, concentration of both organic layers and recrystallization from CH_2Cl_2/*n*-hexane returned 1.2 g **7** (turnover 76 %) and gave 3.14 g **8** (9.86 mmol, 93 % based on consumed **7**). R_f = 0.35 (ethyl acetate/petroleum ether 1:1); $[\alpha]_D^{21}$ = 21.7 (c = 1.09, acetone); mp = 90 °C (CH_2Cl_2/*n*-hexane); ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.630 (d, 1 H, $^2J_{2',2}$ = 18.4, $^3J_{2',3}$ = 0, H-2′), 2.687 (dd, 1 H, $^2J_{2',2}$ = 18.4, $^3J_{2,3}$ = 5.7, H-2), 4.893 (dd, 1 H, $^3J_{2',3}$ = 0, $^3J_{2,3}$ = 5.7, $^3J_{3,4}$ = 3.8, H-3), 4.721 (d, 1 H, $^3J_{3,4}$ = 3.8, $^3J_{4,5}$ = 0, H-4), 4.526 (d, 1 H, $^3J_{4,5}$= 0, $^3J_{5,6}$ = 2.5, H-5), 3.910 (dd, 1 H, $^3J_{5,6}$ = 2.5, $^3J_{6,7}$ = 8.3, H-6), 3.867 (ddd, 1 H, $^3J_{6,7}$ = 8.3, $^3J_{7,8'}$ = 5.1, $^3J_{7,8}$ = 3.2, H-7), 3.693 (dd, 1 H, $^2J_{8',8}$ = 11.4, $^3J_{7,8'}$ = 5.1, H-8′),

3.788 (dd, 1 H, $^2J_{8',8}$ = 11.4, $^3J_{7,8}$ = 3.2, H-8), 0.151, 0.163 (s, 3 H, $Si(CH_3)_2$), 0.901 (s, 9 H, $SiC(CH_3)_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 175.32 (C-1), 36.05 (C-2), 76.98 (C-3), 87.72 (C-4), 75.10 (C-5), 81.27 (C-6), 68.79 (C-7), 64.37 (C-8), -5.04, -4.92 ($Si(\underline{C}H_3)_2$), 25.60 ($SiC(\underline{C}H_3)_3$), 17.93 ($Si\underline{C}(CH_3)_3$); MS: m/z (%) 319 (100) [MH^+]; $C_{14}H_{26}O_6Si$ (318.44): calc. C 52.81, H 8.24, found C 52.59, H 7.98.

2,5-Anhydro-3-*O*-(*tert*-butyldimethylsilyl)-6-deoxy-D-ido-hepturono-7,4-lactone (9): A solution of 1.34 g $NaIO_4$ in 25 ml MeOH/H_2O (2:3) was added dropwise to a cooled solution of 1.0 g **8** (3.14 mmol) in 20 ml MeOH/H_2O (2:1), so that the reaction temperature did not rise over 5 °C. After stirring for a further 30 min at 0 °C the reaction mixture was diluted with CH_2Cl_2 and water and extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave the crude aldehyde **9** which was immediately subjected to Grignard addition without further purification. An analytical pure sample was obtained by column chromatography. R_f = 0.35 (ethyl acetate/petroleum ether 2:5); $[\alpha]_D^{21}$ = -8.7 (c = 1.78, acetone); mp = 72-74 °C (CH_2Cl_2/*n*-hexane); ^1H NMR (500.1 MHz, $CDCl_3$): δ = 9.571 (d, 1 H, $^3J_{1,2}$ = 1.3, H-1), 4.429 (dd, 1 H, $^3J_{1,2}$ = 1.3, $^3J_{2,3}$ = 3.8, H-2), 4.792 (d, 1 H, $^3J_{2,3}$= 3.8, $^3J_{3,4}$ = 0, H-3), 4.721 (d, 1 H, $^3J_{3,4}$ = 0, $^3J_{4,5}$ = 3.8, H-4), 5.137-5.157 (m, 1 H, H-5), 2.737-2.743 (m, 2 H, H-6′, H-6), 0.150, 0.170 (s, 3 H, $Si(CH_3)_2$), 0.912 (s, 9 H, $SiC(CH_3)_3$); ^{13}C NMR (125.5 MHz, $CDCl_3$): δ = 199.61 (C-1), 85.99 (C-2), 78.76 (C-3), 87.57 (C-4), 77.26 (C-5), 36.03 (C-6), 174.30 (C-7), -5.39, -4.97 ($Si(\underline{C}H_3)_2$), 25.43 ($SiC(\underline{C}H_3)_3$), 17.85 ($Si\underline{C}(CH_3)_3$); MS: m/z (%) 287 (100) [MH^+]; $C_{13}H_{22}O_5Si$ (286.40): calc. C 54.52, H 7.75, found C 54.30, H 7.38.

3,6-Anhydro-5-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-7-*C*-phenyl-L-glycero-D-ido-heptono-1,4-lactone (10): 200 mg **9** (0.70 mmol) were dissolved in dry THF (3 ml) and the solution was cooled to – 20 °C under N_2 atmosphere. 0.77 ml of a 1.0 M solution of phenylmagnesium bromide (0.77 mmol) in dry THF were added dropwise. The reaction mixture was allowed to warm up to room temperature within 1.5 h. After addition of saturated aqueous NH_4Cl, the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. Column chromatography of the residue gave 140 mg **10** (0.38 mmol, 55 %) as syrup. R_f = 0.13 (ethyl acetate/petroleum ether 2:5); $[\alpha]_D^{21}$ = 65.1 (c = 1.21, acetone); ^1H NMR (500.1 MHz, $CDCl_3$): δ = 2.680-2.689 (m, 2 H, H-2′, H-2), 5.062-5.085 (m, 1 H, H-3), 4.927 (d, 1 H, $^3J_{3,4}$ = 5.1, $^3J_{4,5}$ = 0, H-4), 4.382 (d, 1 H, $^3J_{4,5}$ = 0, $^3J_{5,6}$ = 3.8, H-5), 4.266 (dd, 1 H, $^3J_{5,6}$ = 3.8, $^3J_{6,7}$ = 4.5, H-6), 4.786 (d, 1 H, $^3J_{6,7}$ = 4.5, H-7), 7.273-7.391 (m, 5 H, H_{phenyl}), 0.030, 0.122 (s, 3 H, $Si(CH_3)_2$), 0.901 (s, 9 H, $SiC(CH_3)_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 175.09 (C-1), 36.08 (C-2), 77.26 (C-3), 88.55 (C-4), 76.56 (C-5), 84.32 (C-6), 72.81 (C-7), 126.93, 128.14, 128.45, 139.69 (C_{phenyl}), -5.26, -4.57 ($Si(\underline{C}H_3)_2$), 25.83 ($SiC(\underline{C}H_3)_3$), 17.88 ($Si\underline{C}(CH_3)_3$); MS: m/z (%) 365 (70) [MH^+], 347 (100) [MH^+-H_2O]; $C_{19}H_{18}O_5Si$ (364.51): calc. C 62.61, H 7.74, found C 62.37, H 7.62.

3,6-Anhydro-2-deoxy-7-*C*-phenyl-L-glycero-D-ido-heptono-1,4-lactone, (+)-7-epi-goniofufurone (2): 60 mg **10** (0.165 mmol) were dissolved in 5 ml dry THF. 4.8 ml dry MeOH were added followed by dropwise addition of 0.20 ml acetyl chloride. The reaction mixture was stirred at room temperature for 12 h. The solvent was removed and the residue was purified by column chromatography yielding 25 mg **2** (0.100 mmol, 60 %).

2 *was also prepared from the reaction of* **15** *with* **3**: 0.60 g **15** (2.63 mmol) was dissolved in DMF and stirred with 0.70 g meldrum's acid (5.26 mmol) and 0.30 ml *tert.*-butylamine (2.63 mmol) at 40 °C for 5 days. The solvent was removed in vacuum using toluene as co-solvent. Column chromatography with ethyl acetate/toluene (1:1) gave 0.59 g **2** (2.37 mmol, 90 %).

R_f = 0.47 (ethyl acetate); $[\alpha]_D^{20}$ = 94.5 (c = 0.66, EtOH); mp = 195-198 °C (ethyl acetate/*n*-hexane 1:1); ^1H NMR (500.1 MHz, DMSO-d_6): δ = 2.460 (d, 1 H, $^2J_{2',2}$ = 18.5, $^3J_{2',3}$ = 0, H-2′), 2.895 (dd, 1 H, $^2J_{2',2}$ = 18.5, $^3J_{2,3}$ = 6.4, H-2), 4.945 (dd, 1 H, $^3J_{2',3}$ = 0, $^3J_{2,3}$ = 6.4, $^3J_{3,4}$ = 4.5, H-3), 4.765 (d, 1 H, $^3J_{3,4}$ = 4.5, $^3J_{4,5}$ = 0, H-4), 3.664 (d, 1 H, $^3J_{4,5}$ = 0, $^3J_{5,6}$ = 3.1, H-5), 3.851 (dd, 1 H, $^3J_{5,6}$ = 3.1, $^3J_{6,7}$

= 7.7, H-6), 4.779 (d, 1 H, $^3J_{6,7}$ = 7.7, H-7), 7.25-7.43 (m, 5 H, H_{phenyl}); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 176.19 (C-1), 36.05 (C-2), 77.80 (C-3), 87.98 (C-4), 73.21 (C-5), 85.09 (C-6), 71.53 (C-7), 127.08, 127.41, 128.05, 142.52 (C_{phenyl}); MS: m/z (%) 251 (67) [MH^+], 233 (100) [MH^+-H_2O]; $C_{13}H_{14}O_5$ (250.25): calc. C 62.40, H 5.64, found C 62.17, H 5.62.

1,2-*O*-Isopropylidene-5-*C*-phenyl-β-L-ido (13) and 1,2-*O*-isopropylidene-5-*C*-phenyl-α-D-gluco-pentofuranose (14): 15.53 g $NaIO_4$ (72.6 mmol) was added to a solution of 1,2-*O*-isopropylidene-α-D-glucofuranose (**11**) (7.99 g, 36.3 mmol) in a 200 ml MeOH/water (2:1) at 0 °C. After 2 days at 4 °C the solvent was evaporated and the resulting residue was dissolved in water (100 ml) and extracted 10 times with ethyl acetate (100 ml each). Drying over $MgSO_4$ and concentration gave an oil which was further dried for 2 h over P_2O_5 at 0.01 mbar. This crude aldehyde was dissolved together with 4.3 g $ZnCl_2$ (32.4 mmol) in dry THF (100 ml) and added dropwise to a solution of phenylmagnesium bromide over 1 h. Phenylmagnesium bromide was prepared immediately prior to use from 3.9 g magnesium tubes (160.0 mmol) and bromobenzene (16.7 ml, 160.0 mmol) in dry THF (150 ml). After stirring at 0 °C for 4 h, the reaction mixture was allowed to reach room temperature over 20 h. Addition of saturated aqueous NH_4Cl (150 ml) and extraction which ethyl acetate (9 x 100 ml), drying ($MgSO_4$) and evaporation of the solvent gave a pale yellow oil. Column chromatography with ethyl acetate / toluene (1:1) as eluent gave **13** (3.0 g, 11.2 mmol, 31%) and **14** (3.0 g 11.2 mmol, 31 %). **13**: R_f = 0.23 (ethyl acetate/toluene 1:1); $[\alpha]_D^{20}$ = 32.1 (c = 1.34, MeOH); mp = 162-165 °C (EtOH); ^1H NMR (500.1 MHz, $CDCl_3$): δ = 5.994 (d, 1 H, $^3J_{1,2}$ = 3.8, H-1), 4.466 (d, 1 H, $^3J_{1,2}$ = 3.8, $^3J_{2,3}$ = 0, H-2), 4.054 (d, 1 H, $^3J_{2,3}$ = 0, $^3J_{3,4}$ = 2.5, H-3), 4.297 (dd, 1 H, $^3J_{3,4}$ = 2.5, $^3J_{4,5}$ = 5.1, H-4), 5.109 (d, 1 H, $^3J_{4,5}$= 5.1, H-5), 7.27-7.47 (m, 5 H, H_{phenyl}), 1.285, 1.440 (s, 3 H, $C(CH_3)_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 104.97 (C-1), 85.42 (C-2), 75.96 (C-3), 82.75 (C-4), 72.57 (C-5), 111.97 ($\underline{C}(CH_3)_2$), 26.19, 26.77 ($C(CH_3)_2$), 126.77, 128.25, 128.61, 140.04 (C_{phenyl}); MS: m/z (%) 249 (100) [MH^+-H_2O]; $C_{14}H_{18}O_5$ (266.29): calc. C 63.15, H 6.81, found C 63.22, H 6.77. **14**: R_f = 0.30 (ethyl acetate/toluene 1:1); $[\alpha]_D^{20}$ = -43.4 (c = 1.33, MeOH); mp = 104-106 °C (EtOH); ^1H NMR (500.1 MHz, $CDCl_3$): δ = 5.971 (d, 1 H, $^3J_{1,2}$ = 3.8, H-1), 4.438 (d, 1 H, $^3J_{1,2}$ = 3.8, $^3J_{2,3}$ = 0, H-2), 4.135 (d, 1 H, $^3J_{2,3}$ = 0, $^3J_{3,4}$ = 2.5, H-3), 4.151 (dd, 1 H, $^3J_{3,4}$ = 2.5, $^3J_{4,5}$ = 2.8, H-4), 5.199 (d, 1 H, $^3J_{4,5}$= 2.8, H-5), 7.27-7.43 (m, 5 H, H_{phenyl}), 1.264, 1.422 (s, 3 H, $C(CH_3)_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 104.81 (C-1), 84.92 (C-2), 75.14 (C-3), 82.10 (C-4), 73.07 (C-5), 111.56 ($\underline{C}(CH_3)_2$), 25.94, 26.55 ($C(CH_3)_2$), 126.00, 128.09, 128.52, 139.61 (C_{phenyl}); MS: m/z (%) 267 (10) [MH^+], 249 (100) [MH^+-H_2O]; $C_{14}H_{18}O_5$ (266.29): calc. C 63.15, H 6.81, found C 63.56, H 6.88.

5-*C*-Phenyl-β-L-ido-pentofuranose (15): 0.97 g **13** (3.7 mmol) were dissolved in 20 ml half concentrated acetic acid and stirred at 80 °C for 25 h. Removal of the solvent under reduced pressure and purification by column chromatography using ethyl acetate as eluent gave 0.8 g **15** (97 %) as syrup. R_f = 0.45 (ethyl acetate); $[\alpha]_D^{20}$ = 43.5 (c = 1.32, water); ^1H NMR (300.1 MHz, D_2O): δ = 5.103 (d, 1 H, $^3J_{1,2}$ = 1.7, H-1), 3.667 (d, 1 H, $^3J_{1,2}$ = 1.7, $^3J_{2,3}$ = 0, H-2), 4.112 (d, 1 H, $^3J_{2,3}$ = 0, $^3J_{3,4}$ = 2.8, H-3), 3.646 (d, 1 H, $^3J_{3,4}$ = 2.8, $^3J_{4,5}$ = 0, H-4), 4.932 (s, 1 H, $^3J_{4,5}$ = 0, H-5), 7.23-7.41 (m, 5 H, H_{phenyl}); ^{13}C NMR (75.5 MHz, D_2O): δ = 93.14 (C-1), 70.40 (C-2), 70.95 (C-3), 69.72 (C-4), 75.73 (C-5), 126.60, 128.73, 128.96, 138.04 (C_{phenyl}); MS: m/z (%) 209 (100) [MH^+-H_2O], 191 (30) [MH^+-$2H_2O$], 173 (12) [MH^+-$3H_2O$]; $C_{11}H_{14}O_5$ (226.23): calc. C 58.40, H 6.24, found C 58.63, H 6.32.

5-*C*-Phenyl-α-D-gluco-pentofuranose (16): 0.97 g **14** (3.7 mmol) were dissolved in 20 ml half concentrated acetic acid and stirred at 80 °C for 25 h. Removal of the solvent under reduced pressure and purification by column chromatography using ethyl acetate as eluent gave 0.8 g **16** (97 %) as white crystals. R_f = 0.14 (ethyl acetate); $[\alpha]_D^{20}$ = 20.1 (c = 1.25, water); ^1H NMR (500.1 MHz, D_2O): δ = 4.937 (d, 1 H, $^3J_{1,2}$ = 8.3, H-1), 3.381 (dd, 1 H, $^3J_{1,2}$ = 8.3, $^3J_{2,3}$ = 8.9, H-2), 3.297 (dd, 1 H, $^3J_{2,3}$ = 8.9, $^3J_{3,4}$ = 8.9, H-3), 3.488 (dd, 1 H, $^3J_{3,4}$ = 8.9, $^3J_{4,5}$ = 9.6, H-4), 3.288 (d, 1 H, $^3J_{4,5}$ = 9.6, H-5), 7.05-7.14 (m, 5 H, H_{phenyl}); ^{13}C NMR (75.5 MHz, D_2O): δ = 92.75 (C-

1), 72.98 (C-2), 74.14 (C-3), 71.94 (C-4), 74.44 (C-5), 128.20, 128.44, 129.10, 137.63 (C_{phenyl}); MS: m/z (%) 209 (100) [MH^+-H_2O], 191 (74) [MH^+-$2H_2O$], 173 (44) [MH^+-$3H_2O$]; $C_{11}H_{14}O_5$ (226.23): calc. C 58.40, H 6.24, found C 58.08, H 6.37.

3,6-Anhydro-2-deoxy-7-*C*-phenyl-D-glycero-D-ido-heptono-1,4-lactone, (+)-goniofufurone (1): 0.60 g **16** (2.63 mmol) was dissolved in DMF and stirred with 0.70 g meldrum's acid (5.26 mmol) and 0.30 ml *tert.*-butylamine (2.63 mmol) at 40 °C for 5 days. The solvent was removed in vacuum using toluene as co-solvent. Column chromatography with ethyl acetate/toluene (1:1) gave 0.59 g **1** (2.37 mmol, 90 %). R_f = 0.57 (ethyl acetate); $[\alpha]_D^{20}$ = 44.9 (c = 1.12, $CHCl_3$), $[\alpha]_D^{20}$ = 9.9 (c = 0.75, EtOH); mp = 147-150 °C (ethyl acetate/*n*-hexane 1:1); ^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 2.645 (d, 1 H, $^2J_{2',2}$ = 18.8, $^3J_{2',3}$ = 0, H-2'), 2.720 (dd, 1 H, $^2J_{2',2}$ = 18.8, $^3J_{2,3}$ = 5.9, H-2), 5.077 (dd, 1 H, $^3J_{2',3}$ = 0, $^3J_{2,3}$ = 5.9, $^3J_{3,4}$ = 4.1, H-3), 4.836 (d, 1 H, $^3J_{3,4}$ = 4.1, $^3J_{4,5}$ = 0, H-4), 4.378 (d, 1 H, $^3J_{4,5}$ = 0, $^3J_{5,6}$ = 2.6, H-5), 4.066 (dd, 1 H, $^3J_{5,6}$ = 2.6, $^3J_{6,7}$ = 4.8. H-6), 5.158 (d, 1 H, $^3J_{6,7}$ = 4.8, H-7), 7.31-7.42 (m, 5 H, H_{phenyl}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 175.26 (C-1), 36.07 (C-2), 77.43 (C-3), 87.45 (C-4), 74.53 (C-5), 82.98 (C-6), 73.54 (C-7), 125.90, 128.50, 128.83, 138.92 (C_{phenyl}); MS: m/z (%) 251 (100) [MH^+]; $C_{13}H_{14}O_5$ (250.25): calc. C 62.40, H 5.64, found C 62.30, H 5.67.

References

1. Wu, Y.C.; Duh, C.Y.; Chang, F.R.; Chang, G.Y.; Wang, S.K.; Chang, J.J.; McPhail, D.R.; McPhail, A.T.; Lee, K.H.; *J. Nat. Prod.* **1991,** *54*, 1077.
2. Talapatra, S.K.; Basu, D.; Deb, T.; Goswami, S.; Talapatra, B.; *Indian. J. Chem., Sect. B.* **1985,** *24*, 29.
3. Sam, T.W.; Yeu, C.S.; Matsjeh, S.; Gan, E.K.; Razak, D.; Mohamed, A.L.; *Tetrahedron Lett.* **1987,** *28*, 2541.
4. Fang, X.P.; Anderson, J.E.; Chang, C.-J.; Fanwick, P.E.; McLaughlin, J.L.; *J. Chem. Soc., Perkin Tras.1* **1990,** 1655.
5. Fang, X.P.; Anderson, J.E.; Chang, C.-J.; McLaughlin, J.L.; *J. Nat. Prod.* **1991,** *54*, 1034.
6. a) Shing, T.K.M.; Tsui, H.-C.; *J. Chem. Soc., Chem. Commun.* **1992,** 432,
   b) Shing, T.K.M.; Tsui, H.-C.; Zhou, Z.-H.; *Tetrahedron* **1992,** *48*, 8659.
7. a) Gracza, T.; Jäger, V.; *Synlett* **1992**, 191,
   b) Gracza, T.; Jäger, V.; *Synthesis* **1994**, 1359.
8. a) Shing, T.K.M.; Tsui, H.C.; Zhou, Z.-H.; *J. Org. Chem.* **1995,** *60*, 3121 and references cited therein,
   b) Mukai, C.; Hirai, S.; Kim, I.J.; Kido, M.; Hanaoka, M.; *Tetrahedron* **1996,** *52*, 6547,
   c) Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T.; *Tetrahedron* **1999,** *55*, 2493 and references cited therein,
   d) Surivet, J.P.; Vatèle, J.-M.; *Tetrahedron Lett.* **1996,** *37*, 4373,
   e) Mereyala, H.B.; Gadikota, R.R.; Krishnan, R.; *J. Chem. Soc., Perkin Trans. 1* **1997,** 3567,
   f) Surivet, J.P.; Vatèle, J.-M.; *Tetrahedron Lett.* **1997,** *38*, 819,
   g) Cagnolini, C.; Ferri, M.; Jones, P.R.; Murphy, P.J.; Ayres, B.; Cox, B.; *Tetrahedron* **1997**, *53*, 4815,
   h) Yi, X.-H.; Meng, Y.; Li, C.-J.; *J. Chem. Soc., Chem. Commun.* **1998**, 449,
   i) Yi, X.-H.; Meng, Y.; Hua, X.-G.; Li, C.-J.; *J. Org. Chem.* **1998**, *63*, 7472.
9. a) Zamora Mata, F.; Martinez, M.B.; Perez, J.A.G.; *Carbohydr. Res.* **1990,** *210*, 223,
   b) Zamora Mata, F.; Martinez, M.B.; Perez, J.A.G.; *Carbohydr. Res.* **1992**, *225*, 159,
   c) Wernicke, A.; Lützen, A.; Kovács, J.; Köll, P.; *Eur. J. Org. Chem.* submitted.
10. Hoye, T.R.; Tan, L.; *Tetrahedron Lett.* **1995,** *36*, **1981.**
11. Richtmyer, N.K.; *Methods in Carbohydrate Chemistry* **1963**, *2*, 320.