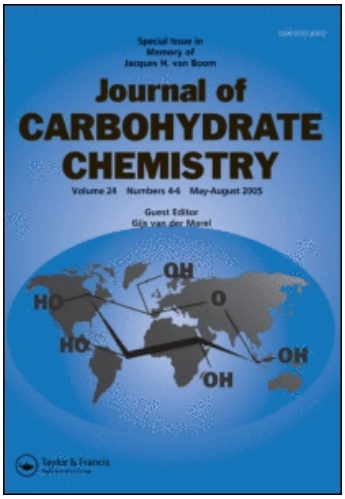

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REGIOSELECTIVE ACYLATIONS OF ALDONO-1,4-LACTONES

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ABSTRACT

Partial benzoylation or pivaloylation of D-gulono-1,4-lactone (**1**) with 3.3-3.6 molar equivalents of the acyl chloride afforded 2,5,6-tri-*O*-benzoyl- (**3**) or 2,5,6-tri-*O*-pivaloyl-D-gulono-1,4-lactone (**5**), which were isolated crystalline from the reaction mixture in yields of 54% and 84.5 %, respectively. Similarly, partial pivaloylation of L-mannono-1,4-lactone (**6**) gave crystalline 2,5,6-tri-*O*-pivaloyl-L-mannono-1,4-lactone (**9**) in 50% yield. Under the same conditions of acylation, D-galactono-1,4-lactone (**11**) gave a mixture of products, which were separated by column chromatography. On benzoylation, 2,3,5,6-tetra-*O*-benzoyl- (**12**); 2,5,6-tri-*O*-benzoyl- (**13**); 2,3,6-tri-*O*-benzoyl- (**14**) and 2,6-di-*O*-benzoyl-D-galactono-1,4-lactone (**15**) were obtained in 47%, 16.4%, 8%, and 14% yield, respectively. Pivaloylation of **11** afforded 2,3,5,6-tetra-*O*-pivaloyl- (**16**), 2,5,6-tri-*O*-pivaloyl- (**17**), 2,3,6-tri-*O*-pivaloyl (**18**) and 2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone (**19**) in 21.6%, 9.7%, 2.6%, and 30.0%, respectively.

INTRODUCTION

Selectively protected aldonolactones are useful intermediates for the synthesis of natural products.[1,2] In this laboratory we have employed partially acylated aldonolactones for the preparation of monomethylated sugars,[3,4] and as glycosylating agents,[5,6] for the construction of naturally occuring disaccharides having immunological activity. In connection with these studies and in order to synthesize 1→3-linked disaccharides and

oligosaccharides, we required large quantities of tri-*O*-acylated derivatives of aldono-1,4-lactones having HO-3 free. Therefore we studied the selective tri-*O*-benzoylation and tri-*O*-pivaloylation of D-gulono-1,4-lactone (**1**), L-mannono-1,4-lactone (**6**), and D-galactono-1,4-lactone (**11**).

RESULTS AND DISCUSSION

Benzoylation of D-gulono-1,4-lactone (**1**) with 3.3 molar equivalents of benzoyl chloride in pyridine at 0 °C for 2 h afforded an amorphous solid, which contained two main products in 4:1 ratio, as determined from its ^{1}H NMR spectrum by integration of the doublets (due to H-2) at δ 5.76 and 6.13. A crystalline product was obtained upon addition of ethyl ether. This product showed the same physical constants[7] as 2,3,5,6-tetra-*O*-benzoyl-D-gulono-1,4-lactone (**2**) and we now report the spectral data for **2** (Tables 1 and 2). From the ether solution 2,5,6-tri-*O*-benzoyl-D-gulono-1,4-lactone (**3**) was isolated in 54% yield. A second crop of crystals (78.8% overall yield) was obtained by column chromatography of the mother liquors. The structures of **2** and **3** were confirmed from their spectral data; the signal for H-3 in the ^{1}H NMR spectrum of **2** showed a large downfield shift (> 1 ppm) with respect to the same signal of **3**, as expected for the benzoylation of HO-3. Also, the signals for the vicinal protons (H-2 and H-4) were somewhat deshielded in **2**. Furthermore, benzoylation of HO-3 caused a downfield displacement of the α-carbon signal but an upfield shift for the β-carbon signals (2.6 and 1.8 ppm for C-2 and C-4, respectively), as observed for the monobenzoylation of other sugar derivatives.[8]

Pivaloylation of D-gulono-1,4-lactone (**1**) with 3.6 equivalents of pivaloyl chloride was higly regioselective, affording the 2,5,6-tri-*O*-pivaloyl derivative **5**, which crystallized from the reaction mixture in ~85% yield. The perpivalate **4** was a minor product (2.6% yield). The pivaloylation of the free HO group of **5** produced, as the benzoylation, characteristic shifts for H-3 and C-3, and for their vicinal proton and carbon atoms signals. The product distribution in both, benzoylation and pivaloylation of **1** (and of the other lactones studied) was temperature dependent. Therefore, the reported conditions are the optimized ones.

The lower reactivity for HO-3 in the benzoylation and pivaloylation of **1** may be attributed to the *gauche* interactions of HO-3 with HO-2 and the bulky side chain on C-4. Furthermore, lactone **1** exists both in solution[9] and in the crystalline state[10] almost exclusively in the $\mathbf{E}_3$ (D) conformation, which has HO-3 in an axial or pseudoaxial disposition, being therefore less reactive.[11]

The same *gauche* interactions of HO-3 with HO-2 and the lateral chain on C-4, and axial orientation for HO-3, were observed for L-mannono-1,4-lactone (**6**) in the preferred[9]

TABLE 1. ^{1}H NMR Spectral Data[a] for Compounds 2-5, 9-10 and 12-19

Compound	H-2	H-3	H-4	H-5	H-6,6'	HO	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
2	6.13	6.32	5.24	5.99	4.82, 4.56		5.2	3.4	7.0	4.0	4.4	12.5
3	5.76	5.01-4.88		5.96	4.86-4.65	3.00	4.0					
4	~5.81		4.80	5.46	4.57, 3.89			2.2	9.4	2.5	3.8	12.7
5	5.52	4.72	4.63	5.50	4.57, 4.30	3.00	4.8	2.8	8.8	2.5	3.9	12.5
9	5.81	5.73	4.78	5.23	4.73, 4.15		4.5	2.7	9.8	2.3	3.2	12.7
10	5.44	4.49	4.42	5.30	4.67, 4.24	3.32	4.4	2.5	9.2	2.2	4.6	12.5
12[b]	6.35	6.20	5.50	6.16	5.05-4.70		6.3	6.3	3.5			
13[b]	6.01	5.06-4.63		5.96	5.06-4.63	5.73	8.0					
13	5.64	4.54	4.71	5.84	4.90-4.71	4.11	7.4	7.4	2.9	6.4	6.4	
14[b]	6.39	6.25	5.14	4.87	4.62-4.45	5.35	6.8	6.7	2.2			
15[b]	6.04	4.94	4.65	4.37	4.65-4.50	4.91, 5.43	8.6	8.6				
16	5.62	5.39	4.57	5.31	4.40, 4.18		7.5	7.2	3.2	4.9	6.7	11.8
17	5.27	4.17	4.43	5.36	4.40, 4.25	3.55	7.6	7.8	3.7	4.4	7.0	11.9
18	5.62		4.38	4.04	4.34, 4.19	2.64			2.2	6.4	5.0	11.6
19	5.28	4.57	4.28	4.08	4.37, 4.23	3.66, 2.70	7.8	7.6	2.5	6.3	4.4	11.9

a. For compounds **7** and **8** see Ref. 12

b. Recorded in acetone-d_6

TABLE 2. ^{13}C NMR Spectral Data for Compounds 2-5, 7-10 and 12-19

Compound	C-1	C-2	C-3	C-4	C-5	C-6
2	169.3	68.5	70.0	76.8	69.3	62.3
3	170.0	71.1	68.4	78.6	70.5	62.6
4	168.8	68.4	69.2	76.5	69.0	60.7
5	170.0	70.2*	68.2	78.5	70.0*	61.9
7	168.8	69.3*	68.5*	75.3	67.9	62.6
8	a	70.8	68.5*	77.1	68.2*	62.7
9	a	68.5	68.5	74.6	66.9	61.3
10	a	70.1*	67.8*	76.8	67.9*	62.1
12[b]	169.1	73.9	74.3	78.9	71.0	63.2
13[b]	169.4	76.3	72.3	79.7	70.5	63.5
14[b]	169.4	74.3*	73.8*	80.4	68.2	65.9
15[b]	169.3	76.2	71.8	81.3	67.3	66.1
16	167.8	71.9	71.9	77.3	68.1	61.8
17	168.1	75.9	72.9	79.3	68.8	62.2
18	168.4	72.6*	72.0*	79.2	68.2	64.4
19	168.8	76.3	72.4	80.7	68.2	64.9

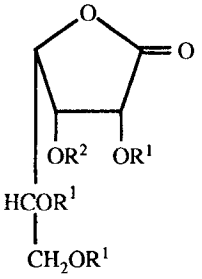
a. Not observed in the conditions used to record the spectrum.

b. Recorded in acetone-d_6

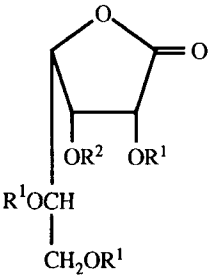
* Signals may be interchanged.

E_3 (L) conformation. Hence, the HO-3 group of **6** should be the least reactive. In fact, partial pivaloylation of **6** under the conditions described for **1**, led to 2,5,6-tri-*O*-pivaloyl-L-mannono-1,4-lactone (**10**), isolated as a crystalline solid from the reaction mixture in 50% yield. Although TLC showed that the mother liquors still contained **10** as the main component, further recovery of this product by column chromatography was not effective, as decomposition was observed. From the column, only a small amount of 2,3,5,6-tetra-*O*-pivaloyl-L-mannono-1,4-lactone (**9**) was isolated. We have previously reported[12] that partial

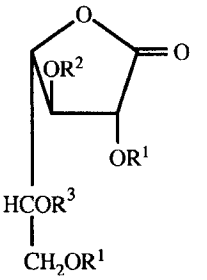
benzoylation of D-mannono-1,4-lactone gave, after separation by column chromatography, the 2,5,6-tribenzoate (**8**) and the perbenzoate (**7**) in 60% and 25% yield, respectively (for simplification formulae **7** and **8** are depicted in the L-series).



1 R^1 =R^2 =H
2 R^1 =R^2 =PhCO
3 R^1 =PhCO, R^2 =H
4 R^1 =R^2 =Bu^{t}CO
5 R^1 =Bu^{t}CO, R^2 =H



6 R^1 =R^2 =H
7 R^1 =R^2 =PhCO
8 R^1 =PhCO, R^2 =H
9 R^1 =R^2 =Bu^{t}CO
10 R^1 =Bu^{t}CO, R^2 =H



11 R^1 =R^2 =H
12 R^1 =R^2 =R^3 =PhCO
13 R^1 =R^3 =PhCO, R^2 =H
14 R^1 =R^2 =PhCO, R^3 =H
15 R^1 =PhCO, R^2 =R^3 =H
16 R^1 =R^2 =R^3=Bu^{t}CO
17 R^1 =R^3 =Bu^{t}CO, R^2 =H
18 R^1 =R^2 =Bu^{t}CO, R^3 =H
19 R^1 =Bu^{t}CO, R^2 =R^3 =H

Differences in the product distribution of benzoylation and pivaloylation of D-gulono-1,4-lactone (**1**) and L-mannono-1,4-lactone (**6**) result from the different configuration of C-5. The larger proportion of 2,5,6-tri-*O*-acyl derivatives **3** and **5**, with respect to **8** and **10**, would suggest a lower reactivity of HO-3 in **1** than in **6**.

Due to the relative stereochemistry of HO-3 in D-galactono-1,4-lactone (**11**) a poor selectivity in partial acylations should be expected. Compound **11** populates mainly, in solution[9] and in the crystalline state,[13] the $\mathbf{E}_3$ (D) conformation, which has HO-3 equatorially oriented and *trans*-disposed with respect to HO-2 and the lateral chain at C-4. Thus, benzoylation of **11** with 3.3 equivalents of benzoyl chloride afforded a mixture which showed by TLC four main spots having Rf 0.59, 0.43, 0.39 and 0.14 (solvent A), later determined to correspond to the perbenzoate **12**, the tribenzoates **13** and **14**, and the dibenzoate **15**, respectively. The ^{13}C NMR of the crude mixture in acetone *d*-6 was employed for an approximate quantification of the composition of the mixture. For this

purpose the procedure of Horton and Walaszek was used,[14] in which the relative intensity of the C-4 signals for each compound in the mixture was determined. The chemical shift of C-4 for each individual compound (**12**-**15**) was obtained from the ^{13}C NMR spectrum of the isolated compounds. The ratio of **12**:**13**:**14**:**15** was 4.3:2.3:1.5:1 (δ_{C-4}: 78.9, 79.7, 80.4 and 81.3, respectively). The addition of diethyl ether to the reaction mixture resulted in the crystalization of the minor, more polar component, 2,6-di-*O*-benzoyl-D-galactono-1,4-lactone (**15**). Compound **15** could be obtained[6] in 62% yield by benzoylation of **11** with 2.2 equivalents of benzoyl chloride under controlled conditions. The other components of the mixture were separated by column chromatography. The 2,3,5,6-tetra-*O*-benzoyl-D-galactono-1,4-lactone (**12**) eluted first (47.5% yield), and the two tri-*O*-benzoyl derivatives (**13** and **14**) were then isolated. From the last fractions of the column an additional amount of **15** (14% overall yield) was obtained. The structures of **13** and **14** were established on the basis of their spectroscopic data. Thus, the less polar tribenzoate (Rf 0.43) was characterized as 2,3,6-tri-*O*-benzoyl-D-galactono-1,4-lactone (**14**), since the most downfield shifted signal of **14** was that of H-3 (1.3 ppm) with respect to the same signal of the dibenzoate **15**. Also, comparing the ^{13}C NMR spectra of **15** with that of **14** we observed a downfield shift for the C-3 signal, but an upfield displacement for the C-2 and C-4 signals of **14**, which confirms that the third benzoate is located on C-3.

The other tri-*O*-benzoylated product (Rf 0.39) was identified as 2,5,6-tri-*O*-benzoyl-D-galactono-1,4-lactone (**13**), obtained crystalline in 16.4% yield. The structure of **13** was determined by comparing their ^{1}H and ^{13}C NMR spectra with those of **14** and **15**. For example, the H-5 signal for **13** appeared at δ 5.84, shifted downfield by ~1 ppm and 1.5 ppm the same signals of **14** and **15**, respectively. The characteristic shifting for the α and β carbon atoms in the ^{13}C NMR spectra of **13**, **14** and **15** also confirmed that the HO-3 of **13** remained free.

Pivaloylation of D-galactono-1,4-lactone (**11**) with 3.3 molar equivalents of pivaloyl chloride gave similar results as benzoylation. Thus, from the reaction mixture, the 2,6-dipivalate **19** crystallized upon addition of hexane (30% yield). The mother liquors were concentrated and chromatographically fractionated affording 2,3,5,6-tetra-*O*-pivaloyl-D-galactono-1,4-lactone (**16**, 21.6% yield), 2,3,6-tri-*O*-pivaloyl-D-galactono-1,4-lactone (**18**, 2.6% yield) and 2,5,6-tri-*O*-pivaloyl-D-galactono-1,4-lactone (**17**, 9.7% yield). The structures of these products were assigned on the basis of their spectroscopic data, as already described for the selective benzoylation of **11**.

From the results on the selective tri-*O*-benzoylation and tri-*O*-pivaloylation of D-gulono- (**1**), L-mannono- (**6**) and D-galactono-1,4-lactone (**11**), we conclude that tri-*O*-acylated derivatives having HO-3 free can be readily obtained in high yields and in

crystalline form from the 1,4-lactones having *gulo* (**1**) and *manno* (**6**) configurations. However, these procedures are not convenient in the case of D-galactono-1,4-lactone (**11**) as large amounts of di-*O*- and per-*O*- acylated derivatives were obtained, and the desired tribenzoate or tripivalate having HO-3 free were isolated after column chromatography, in poor yields.

EXPERIMENTAL

General Procedures. Melting points were determined with a Thomas-Hoover apparatus, and are reported uncorrected. Optical rotations were determined with a Perkin-Elmer 141 polarimeter. The ^1H NMR spectra were recorded using a Varian XL-100 or Varian 300 Gemini spectrometer, at 100 and 300 MHz, respectively. The ^{13}C NMR spectra were performed at 25.2 MHz using a Varian XL-100 spectrometer; assignments were made, when possible, by selective heteronuclear decoupling experiments. The solvent employed for recording the spectra was $CDCl_3$, unless otherwise indicated, and Me_4Si was the internal standard (δ 0.00). Thin layer chromatography (TLC) was performed on Silica Gel 60 F-254 (Merck) precoated plates, with the following solvent systems: 4:1 toluene-EtOAc.(solvent A) and 2:1 hexane-EtOAc (solvent B). Detection was effected by spraying the plates with 5% H_2SO_4 in EtOH (v/v) and charring. For column chromatography silica gel 60 (Merck) was used.

Partial Benzoylation of D-Gulono-1,4-lactone (1). Synthesis of 2,3,5,6-Tetra-*O*-benzoyl-D-gulono-1,4-lactone (2) and 2,5,6-Tri-*O*-benzoyl-D-gulono-1,4-lactone (3). To a stirred solution of D-gulono-1,4-lactone (**1**, 3.57 g, 20.05 mmol) in dry pyridine (30 mL), cooled in an ice-water bath, benzoyl chloride (7.75 mL, 66.2 mmol) was slowly added. The mixture was stirred for 2 h at 0 °C, and then poured into ice-water (200 mL). After 2 h the syrupy product was decanted and dissolved in CH_2Cl_2. The organic solution was washed with satd aq $NaHCO_3$ (100 mL) and satd aq NaCl (2 x 100 mL), dried ($MgSO_4$) and the solvent evaporated to afford an amorphous solid. Addition of ethyl ether (130 mL) to the solid led to a crystalline product (10.0 g), which showed (solvent A) two main spots of Rf 0.41 (major) and Rf 0.54 on TLC. The mother liquors were concentrated and the residue crystallized from EtOH (12 mL) to yield 2,3,5,6-tetra-*O*-benzoyl-D-gulono-1,4-lactone (**2**, 0.53 g, 4.5%); mp 154-155 °C, $[\alpha]_D$ -88.0° (*c* 1.2, $CHCl_3$), Rf 0.54 (solvent A). Lit.[7] mp 155-156 °C, $[\alpha]_D$ -89.3°. The crystalline mass (10.0 g) obtained from ethyl ether, was dissolved in boiling EtOH (50 mL). Upon cooling a crystalline mass (3.81 g) precipitated. TLC of the solid and the mother liquors showed that the former was a 2:1 mixture of the compounds having Rf 0.41 and 0.54, respectively. The

mother liquors showed the presence of the product of Rf 0.41. Evaporation of the EtOH afforded a solid, which crystallized from benzene to yield 2,5,6-tri-*O*-benzoyl-D-gulono-1,4-lactone (**3**, 5.30 g, 54%); mp 83-84 °C, $[\alpha]_D$ -65.3° (*c* 2, acetone). Compound **3** was also isolated by flash chromatography (5:1 toluene-EtOAc) of the mixture (3.81 g) which had precipitated from EtOH. Crystalline **3** (2.43 g, 24.8 %) was obtained; overall yield 78.8%.

Anal. Calcd for $C_{27}H_{22}O_9$: C, 66.12; H, 4.52. Found: C, 66.10; H, 4.61.

Partial Pivaloylation of D-Gulono-1,4-lactone (1). Synthesis of 2,3,5,6-Tetra-*O*-pivaloyl-D-gulono-1,4-lactone (4) and 2,5,6-Tri-*O*-pivaloyl-D-gulono-1,4-lactone (5). To a cooled solution (-20 °C) of D-gulono-1,4-lactone (**1**, 0.53 g, 3.0 mmol) in dry pyridine (10 mL) was slowly added pivaloyl chloride (1.33 mL, 10.8 mmol) in 0.2 mL portions during *ca.* 2 h. The stirred reaction mixture was maintained at 0 °C for 3 h and then stored at room temperature for an additional 20 h. The mixture was poured into ice-water (100 mL) and the resulting syrup was dissolved in CH_2Cl_2 (100 mL). The extract was sequentially washed with 1M HCl (2 x 50 mL), water (50 mL) and sat aq $NaHCO_3$ (2 x 50 mL), dried ($MgSO_4$) and concentrated. The residue crystallized upon addition of hexane, to give 2,5,6-tri-*O*-pivaloyl-D-gulono-1,4-lactone (**5**, 1.10 g, 84.5%). After recrystalization from MeOH-water, **5** had mp 146-148 °C, $[\alpha]_D$ -53° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{21}H_{34}O_9$: C, 58.59; H, 7.96. Found: C, 59.04; H, 7.73.

On concentration of the hexane solution to a small volume (~10 mL) a crop of crystalline 2,3,5,6-tetra-*O*-pivaloyl-D-gulono-1,4-lactone (**4**, 40 mg, 2.6%) was obtained. It had mp 175-177 °C, $[\alpha]_D$ -24.2 ° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{26}H_{42}O_{10}$: C, 60.68; H, 8.23. Found: C,60.87; H, 8.37.

Partial Pivaloylation of L-Mannono-1,4-lactone (6). Synthesis of 2,3,5,6-Tetra-*O*-pivaloyl-L-mannono-1,4-lactone (9) and 2,5,6-Tri-*O*-pivaloyl-L-mannono-1,4-lactone (10). L-Mannono-1,4-lactone (**6**, 0.53 g, 3.0 mmol) was pivaloylated employing the procedure described for the pivaloylation of **1**. The residue remaining after concentration of the CH_2Cl_2 extract slowly crystallized from hexane on storage overnight at 0 °C, affording 2,5,6-tri-*O*-pivaloyl-L-mannono-1,4-lactone (**10**, 0.64 g, 50%), which recrystallized from MeOH-water gave mp 126-128 °C, $[\alpha]_D$ -61.2° (*c* 1, $CHCl_3$), Rf 0.54 (solvent B).

Anal. Calcd for $C_{21}H_{34}O_9$: C, 58.59; H, 7.96. Found: C, 58.55; H,7.96.

The mother liquors remaining from the crystallization of **10** were concentrated and the residue was chromatographed using 19:1 toluene-EtOAc as eluant. The faster moving product (Rf 0.67, solvent B) was 2,3,5,6-tetra-*O*-pivaloyl-L-mannono-1,4-lactone (**9**, 0.10 g, 6.5%). After recrystallization from MeOH-water, compound **9** had mp 159-161 °C, $[a]_D$ -17.4° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{26}H_{42}O_{10}$: C, 60.68; H, 8.23. Found: C, 60.97; H, 8.06.

No other partially pivaloylated derivatives of **6** were isolated as decomposition and pivaloyl migration takes place in contact with the silica gel of the column.

Partial Benzoylation of D-Galactono-1,4-lactone (11). Synthesis of 2,3,5,6-Tetra-*O*-benzoyl-D-galactono-1,4-lactone (12); 2,5,6-Tri-*O*-benzoyl-D-galactono-1,4-lactone (13); 2,3,6-Tri-*O*-benzoyl-D-galactono-1,4-lactone (14) and 2,6-Di-*O*-benzoyl-D-galactono-1,4-lactone (15). To a stirred solution of D-galactono-1,4-lactone (**11**, 1.0 g, 5.6 mmol) in pyridine, externally cooled with an ice-water bath, benzoyl chloride (2.17 mL, 18.53 mmol) was slowly added. After 2 h of stirring at 0 °C the reaction mixture was processed as described for the partial benzoylation of D-gulono-1,4-lactone (**1**), and the syrup obtained showed by TLC (solvent A) four main spots of Rf 0.59, 0.43, 0.39, and 0.14. Upon addition of ethyl ether a crystalline product (Rf 0.14) was obtained and characterized as 2,6-di-*O*-benzoyl-D-galactono-1,4-lactone (**15**, 0.14 g, 6.2%), mp 194-195 °C and $[\alpha]_D$ +3° (*c* 0.8, acetone), as previously reported.[6] The ether solution was concentrated and the resulting syrup was chromatographed on a silica gel column (4 x 20 cm) with 6:1 toluene-EtOAc as eluent. Fractions containing the product having Rf 0.59 were concentrated affording syrupy 2,3,5,6-tetra-*O*-benzoyl-D-galactono-1,4-lactone (**12**, 1.6 g, 47.5%), $[\alpha]_D$ +26° (*c* 1.1, $CHCl_3$). Lit.[15] $[\alpha]_D$ +22.3°.

From the next fraction (Rf 0.43) 2,3,6-tri-*O*-benzoyl-D-galactono-1,4-lactone (**14**, 0.22 g, 8%) was isolated as an amorphous solid, $[\alpha]_D$ +50.4° (*c* 0.5, acetone).

Anal. Calcd for $C_{27}H_{22}O_9$: C, 66.12; H, 4.52. Found: C, 66.25, H, 4.69.

Further elution of the column led to the product having Rf 0.39, which was obtained crystalline (0.45 g, 16.4%). After recrystallization from EtOH, the 2,5,6-tri-*O*-benzoyl-D-galactono-1,4-lactone (**13**) had a mp 121-122 °C, $[\alpha]_D$ -12.0° (*c* 1, acetone).

Anal. Calcd for $C_{27}H_{22}O_9$: C, 66.12; H, 4.52. Found: C,66.16; H, 4.62.

The last fractions from the column afforded an additional amount (0.17 g) of compound **15** (overall yield 14 %).

Partial Pivaloylation of D-Galactono-1,4-lactone (11). Synthesis of 2,3,5,6-Tetra-*O*-pivaloyl-D-galactono-1,4-lactone (16); 2,5,6-Tri-*O*-pivaloyl-D-galactono-1,4-lactone (17); 2,3,6-Tri-*O*-pivaloyl-D-galactono-1,4-lactone (18) and 2,6-Di-*O*-pivaloyl-D-galactono-1,4-lactone (19). To a solution of **11** (1.07 g, 6.0 mmol) in pyridine (20 mL) at -15 °C (ethylene glycol - solid carbon dioxide), pivaloyl chloride (2.66 mL, 21.6 mmol) was added in 0.3 mL portions during 2 h. The reaction mixture was stirred at 0 °C for a further 3 h, and then poured into ice-water (200 mL). The precipitated syrup dissolved in CH_2Cl_2, was washed as described above and the solution concentrated. The residue partially crystallized upon addition of hexane, affording pure 2,6-di-*O*-pivaloyl-D-galactono-1,4-lactone (**19**, 0.62 g, 30%), which after recrystallization from MeOH-water had a mp 133-134 °C, $[\alpha]_D$ -63,7° (*c* 1, $CHCl_3$), Rf 0.25 (solvent B).

Anal. Calcd for $C_{16}H_{26}O_8$: C, 55.48; H, 7.57. Found: C, 55.09; H, 7.17.

The hexane solution, which showed by TLC (solvent B) three main spots of Rf 0.57, 0.45 and 0.41, was concentrated and chromatographically fractionated using 6:1 hexane-EtOAc as eluent. The first fraction contained the faster moving component (Rf 0.57), 2,3,5,6-tetra-*O*-pivaloyl-D-galactono-1,4-lactone (**16**, 0.67 g, 21.6%), which after recrystallization from MeOH-water had a mp 95-96 °C, $[\alpha]_D$ -22.8° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{26}H_{42}O_{10}$: C, 60.68; H, 8.23. Found: C, 60.87; H, 8.37.

From the second fraction (Rf 0.45) 2,3,6-tri-*O*-pivaloyl-D-galactono-1,4-lactone (**18**, 66 mg, 2.6%) was obtained; recrystallized from MeOH-water it gave a mp 113-114 °C, $[\alpha]_D$ -34.8° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{21}H_{34}O_9$: C, 58.59; H, 7.96. Found: C, 58.67; H, 7.48.

The last fraction (Rf 0.41) contained 2,5,6-tri-*O*-pivaloyl-D-galactono-1,4-lactone (**17**, 0.25 g, 9.7%); recrystallized from MeOH-water it gave a mp 95-96 °C, $[\alpha]_D$ -18.9° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{21}H_{34}O_9$: C, 58.59; H, 7.96. Found: C, 58.88; H, 7.90.

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