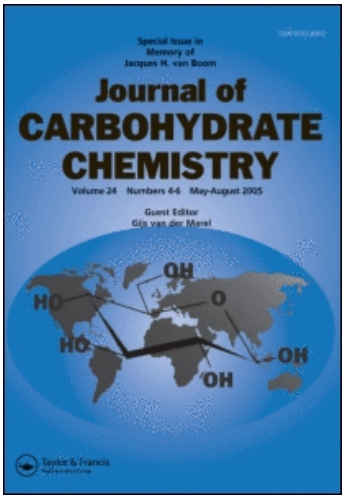


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# C-4 EPIMERIZATION OF α-D-GLUCOPYRANOSIDE: A FACILE SYNTHESIS OF 4-*O*-ACETYL-α-D-GALACTOPYRANOSYL DERIVATIVES

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# C-4 EPIMERIZATION OF α-D-GLUCOPYRANOSIDE: A FACILE SYNTHESIS OF 4-*O*-ACETYL-α-D-GALACTOPYRANOSYL DERIVATIVES

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## ABSTRACT

An unexpected epimerization resulting from the reaction of α-D-glucopyranosyl derivatives with DAST is described. The reaction of 3,4-di-*O*-acetyl-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (**1**), methyl 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (**6**), 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranosyl 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (**13**), and 2,3-di-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-glucopyranosyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**14**) with DAST at 0°C did not give the expected C-4 fluorodeoxy *galacto* derivatives, but instead, the corresponding 4-*O*-acetyl-3-hydroxy-α-D-galactopyranosides in yields of 52–78%. When the treatment of **6** was carried out at −25°C for ~5 min the corresponding diastereomeric 4-*O*-diethylaminosulfinates (**9a,b**) were isolated as the major products (40%). Evidence suggests that the epimerization reaction most probably resulted from an intramolecular displacement of the intermediate diethylaminosulfur difluoride ester or diethylaminosulfinyl ester by the neighbouring acetoxy groups.

## INTRODUCTION

The synthesis of fluorinated carbohydrates has been a subject of special interest in view of their activity in biological systems. Diethylaminosulfur trifluoride (DAST) is a widely used fluorinating reagent with broad application in carbohydrate chemistry.[1,2] It is a convenient method since it effects direct displacement of

the hydroxyl group. The mechanism has been proposed[1] to involve the conversion of a hydroxyl group to an activated species (—$OSF_2NEt_2$), which then undergoes an $S_N2$ substitution reaction by fluoride ion. Consequently, an inversion of configuration will be observed at the reaction center.

In our attempt to synthesize 4-deoxyfluoro galactopyranosyl derivatives by direct fluorination of 2,3,6-acylated glucopyranosyl derivatives using DAST, we found that fluorination did not occur. Instead, we obtained a product in which the neighbouring acetoxy group(s) is involved in an intramolecular nucleophilic displacement reaction to give the 4-*O*-acetyl-3-hydroxy-α-D-*galacto* derivative. This paper reports the results of the reaction of DAST with partially acetylated mono- and disaccharides as a synthetically viable pathway towards obtaining 4-*O*-acetyl-α-D-galactopyranosyl derivatives from the corresponding 3-*O*-acetyl-α-D-glucopyranosides.



## RESULTS AND DISCUSSION

When 3,4-di-*O*-acetyl-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside[3] (**1**) was treated with DAST in dichloromethane at 0°C for about 2 h, the major product (58%) obtained was 3,4-di-*O*-acetyl-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,4,6-tri-*O*-acetyl-α-D-galactopyranoside (**2**). The $^1$H NMR spectra of **2** and its benzoate **3** clearly showed that these compounds had the *galacto* configuration. In both compounds, H-4 appears as a doublet (δ 5.21, 5.58, and $J_{3,4}$ 3.0, 3.1, respectively). A similar observation had been reported[4] for 2-(acetoxymethyl)myoinositol. When the reaction was carefully monitored by TLC, it was observed that, in addition to **2**, there were two other minor compounds, a faster moving compound (than the starting sugar) **4**, and another which had an $R_F$ value very close to that of the starting sugar **2**. Compound **4** was shown by $^1$H and $^{13}$C NMR to be 3,4-di-*O*-acetyl-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-α-D-galactopyranoside. This product must have resulted from the attack of the acetyl group at C-6. The second product was difficult to purify as its $R_F$ value is very close to that of **2**, but repeated column separation gave a small pure sample. This was shown to be 3,4-di-*O*-acetyl-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-galactopyranoside[5] (**5**).

Koch and Chambers[6] reported that reaction of DAST with methyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside at ambient temperature for 18 h in the presence of dimethylaminopyridine (DMAP) gave the 4-fluorodeoxy *galacto* derivative (39%). However, we found that when the reaction was carried out in the absence of DMAP, methyl 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside[7] (**6**) did not give any C-4 fluorodeoxy derivative but instead gave mainly (72%) methyl 2,4-di-*O*-acetyl-6-*O*-trityl-α-D-galactopyranoside (**7**) after about 1 h at 0°C. The *galacto* configuration of **7** and its benzoate **8** were evident from their $^1$H NMR spectra.

Careful monitoring of the reaction by TLC revealed that after about 5 min, a fast-moving compound ($R_F$ = ~0.7) was observed to be formed. This gradu-



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ally decreased in amount as a slower moving compound began to be formed. Hence, it appears that treatment of **6** with DAST at −25°C, initially formed an alkoxy-diethylaminosulfur difluoride intermediate which then underwent partial hydrolysis to give the corresponding sulfinates **9a,b**; if the temperature was kept low (0–5°C) during work-up these products were isolated in >40% yield. At higher temperatures, the major product is **7**, indicating that the diastereomeric sulfinates also undergo similar nucleophilic attack by neighbouring acetoxy group(s) (Scheme 1). $^{1}H$, $^{13}C$, $^{19}F$ NMR and MS studies of **9a,b** showed it to be a mixture of diastereomers. Their $^{1}H$ and $^{13}C$ NMR spectra were consistent with the proposed structures. In addition, the spectra also showed nearly identical peak-intensities and chemical shifts. Biollaz and Kalvoda[8] had reported similar observations in their work on synthesis of fluorinated steroids using DAST.

The above data can be explained *via* a mechanistic pathway similar to that proposed by Yang and Beattie.[4] Thus, reaction of DAST with **1**, for example, initially produces a transient labile ester (**10**), which is rather unreactive. This situation has been reported[10] to commonly arise when nucleophilic attack is sterically hindered and in our case, the nucleophile is approaching from the axial direction. We did not encounter any difficulty when fluorinating C-4 of *galacto* analogues of sucrose and methyl-α-D-galactopyranoside using DAST.[9] It thus appears that as the displacement by the fluoride is difficult, the fluoride nucleophile is able to diffuse away.[10] The diethylamino sulfinate **9** or its precursor **10** then undergoes intramolecular nucleophilic displacement by neighbouring acetoxy groups (at C-3 and C-6) *via* stable 1,3-dioxolan-2-ylium (**11**) and 1,3-dioxan-2-ylium ions (**12**), with inversion of configuration at C-4 (Scheme 1). Ions **11** and **12** are not attacked by fluoride ion in the reaction medium but upon work-up, are attacked by water to give the isolated products. The stereoselectivity of the hydrolysis of **11** and **12** can be rationalized in terms of steric and stereoelectronic factors.[11]

When 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranosyl 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (**13**) and 2,3-di-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-glucopyranosyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**14**) were similarly treated with DAST the expected products, 2,4-di-*O*-acetyl-6-*O*-trityl-α-D-galactopyranosyl 2,4-di-*O*-acetyl-6-*O*-trityl-α- D-galactopyranoside (**15**), and 2,4-di-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranosyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (**16**) were obtained in yields of >70%. Benzoylation of **15** and **16** gave the respective 3-benzoate **17** and **18**. When the reaction of **13** was quenched after about 30 min, the asymmetric α,α-trehalose derivative, 2,4-di-*O*-acetyl-6-*O*-trityl-α-D-galactopyranosyl 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (**19**), was isolated in over 40% yield.

The results discussed above offer a viable synthetic route to compounds, which are problematic to synthesize by alternative methods. It also provides a facile route to obtaining *gluco,galacto* and *galacto,galacto* analogues of α,α-trehalose.





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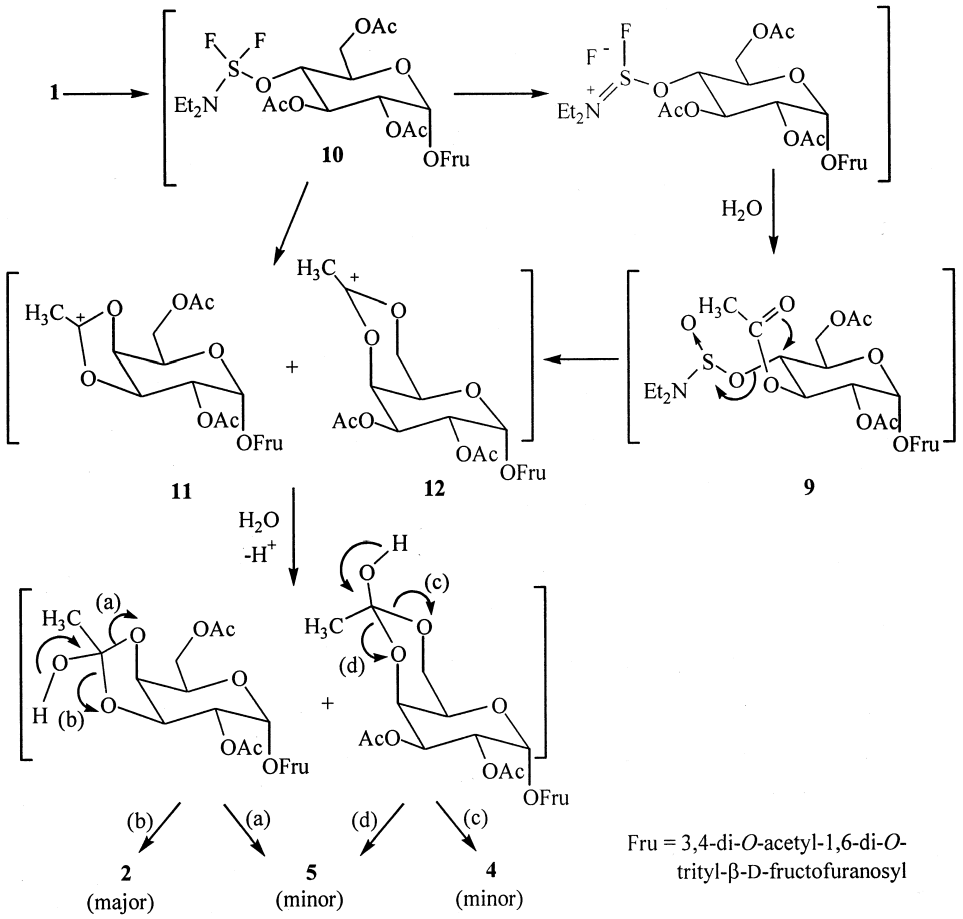


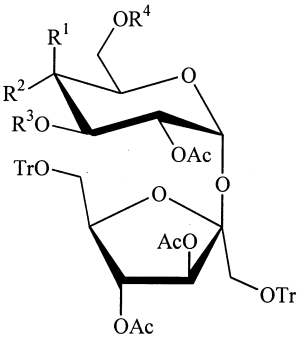

*Scheme 1.*

## EXPERIMENTAL

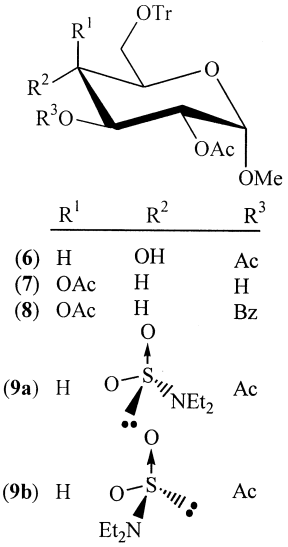
**General Methods.** Melting points were measured with a Thermo Galen Hot Stage Microscope. Optical rotations were taken with a Perkin Elmer 241 polarimeter at 26°C. NMR spectra were recorded at 298 K in $CDCl_3$ (unless otherwise specified) on a Bruker DPX 300 spectrometer (300.13 MHz for $^1H$ and 75.47 MHz for $^{13}C$). Flash chromatography was performed on Silica Gel 60 (0.63–0.200 nm, Merck). Thin-layer chromatography was run on glass plates precoated with silica gel $60F_{254}$ (Merck, Darmstadt, Germany); detection was effected by observation under short wavelength UV light (254 nm), then spraying with 10% sulphuric acid in ethanol and charring them on a hot plate.

**Reaction of 3,4-di-*O*-acetyl-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside with DAST at 0°C.** To a solution of (**1**) (0.33 g, 0.318 mmol) in dichloromethane (15 mL) was added DAST (0.10 mL, 0.763

mmol) drop-wise at 0°C under an argon atmosphere. After 2 h TLC (ether/hexane, 3:1) showed the presence of a major compound and traces of two other compounds. The reaction mixture was washed with satd $NaHCO_3$ solution, brine, then dried ($Na_2SO_4$) and concentrated. Flash column chromatography (ether/hexane, 3:1) gave, first **4** (0.030 g, ~10%) as a colorless syrup: $[\alpha]_D$ +53.9° (*c* 0.48, $CHCl_3$); $^1$H NMR: δ 7.14–7.41 (m, 30H, Ar-*H*), 5.87 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 5.78 (t, 1H, $J_{3',4'} = J_{4',5'}$ 8.4 Hz, H-4′), 5.67 (d, 1H, $J_{3',4'}$ 8.4 Hz, H-3′), 5.32 (d, 1H, $J_{3,4}$ 3.0 Hz, H-4), 5.11 (dd, 1H, $J_{2,3}$ 11.0 $J_{3,4}$ 3.0 Hz, H-3), 4.97 (dd, 1H, $J_{1,2}$ 3.8 $J_{2,3}$ 11.0



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| (**1**) | H | OH | Ac | Ac |
| (**2**) | OAc | H | H | Ac |
| (**3**) | OAc | H | Bz | Ac |
| (**4**) | OAc | H | Ac | H |
| (**5**) | OH | H | Ac | Ac |



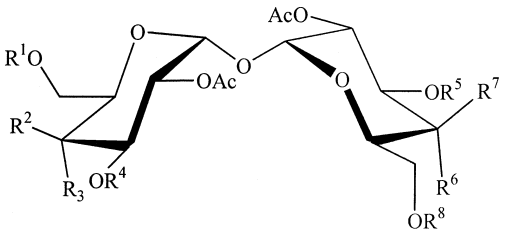
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (**6**) | H | OH | Ac |
| (**7**) | OAc | H | H |
| (**8**) | OAc | H | Bz |



(**9a**) H Ac



(**9b**) H Ac



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | $R^8$ |
|---|---|---|---|---|---|---|---|---|
| (**13**) | Tr | H | OH | Ac | Ac | OH | H | Tr |
| (**14**) | $^t$BuPh$_2$Si | H | OH | Ac | Ac | OAc | H | Ac |
| (**15**) | Tr | OAc | H | H | H | H | OAc | Tr |
| (**16**) | $^t$BuPh$_2$Si | OAc | H | H | Ac | OAc | H | Ac |
| (**17**) | Tr | OAc | H | Bz | Bz | H | OAc | Tr |
| (**18**) | $^t$BuPh$_2$Si | OAc | H | Bz | Ac | OAc | H | Ac |
| (**19**) | Tr | OAc | H | H | Ac | OH | H | Tr |





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Hz, H-2), 4.02–4.29 (m, 2H, H-5,5′), 3.02–3.66 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b) and 1.73, 1.88, 1.92, 2.01, 2.08 (5s, 15H, 5×$CH_3$). $^{13}$C NMR: δ 170.7, 170.2, 170.0, 169.6 (*C*O$CH_3$), 143.6, 143.5, 128.8, 127.8, 127.1 (Ar-*C*), 103.5 (C-2′), 88.7 (C-1), 87.3, 87.1 (*C*$Ph_3$), 78.0 (C-5′), 75.1 (C-3′), 72.9 (C-4′), 70.3 (C-5), 69.2 (C-3), 67.8, 67.2 (C-2,4), 64.2 (C-6), 62.2 (C-6′), 61.9 (C-1′) and 20.8, 20.7, 20.6, 20.5 (CO*C*$H_3$). EI-MS *m/z* (%): 289 [M − $C_{48}H_{43}O_8$]$^+$ (5), 243 (92), 205 (91), 43 (100). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 1059.3779. Found: 1059.3787.

Eluted second was **5** (0.032 g, ∼10%) as a colorless syrup: $[\alpha]_D$ +70.5° (*c* 1.21, $CHCl_3$); $^1$H NMR: δ 7.21–7.51 (m, 30H, Ar-*H*), 5.84 (d, 1H, $J_{3',4'}$ 7.3 Hz, H-3′), 5.56 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 5.37 (t, 1H, $J_{3',4'} = J_{4',5'}$ 7.3 Hz, H-4′), 5.14 (dd, 1H, $J_{1,2}$ 3.7 $J_{2,3}$ 10.8 Hz, H-2), 5.05 (dd, 1H, $J_{2,3}$ 10.8 $J_{3,4}$ 2.7 Hz, H-3), 4.10–4.36 (m, 4H, H-5,5′,6′a, b), 4.02 (d, 1H, $J_{3,4}$ 2.7 Hz, H-4), 3.33–3.52 (m, 2H, H-6′a,b), 3.20 (s, 2H, H-1′a,b) and 1.83, 1.92, 1.94, 1.99, 2.10 (5s, 15H, 5×$CH_3$). $^{13}$C NMR: δ 170.7, 170.2, 170.0, 169.6, 169.6 (*C*O$CH_3$), 143.6, 143.5, (Ph-C), 128.8, 128.7, 127.9, 127.8, 127.1, 127.0 (Ar-*C*), 103.5 (C-2′), 88.7 (C-1), 87.3, 87.1 (*C*$Ph_3$), 78.0 (C-5′), 75.1 (C-3′), 72.9 (C-4′), 70.3 (C-5), 69.2 (C-4), 67.8, 67.2 (C-2,3), 64.3 (C-6), 63.8, 62.1 (C-1′,6′) and 20.8, 20.7, 20.5, 20.4 (CO*C*$H_3$). EI-MS *m/z* (%): 1036[M$^+$] (<0.5), 731 [M − $C_{12}H_{17}O_9$]$^+$ (<0.5), 289 [M–$C_{48}H_{43}O_8$]$^+$ (6), 244 (32), 243 (100), 242 (26), 228 (9), 215 (6), 43 (100).

Anal.Calcd for $C_{60}H_{60}O_{16}$: C, 69.49; H, 5.83. Found: C, 69.87; H, 5.46.

Eluted last was **2** (0.193 g, 58%) as a colorless syrup: $[\alpha]_D$ +58.1° (*c* 0.93, $CHCl_3$); $^1$H NMR: δ 7.22–7.48 (m, 30H, Ar-*H*), 5.81 (d, 1H, $J_{3',4'}$ 7.3 Hz, H-3′), 5.59 (t, 1H, $J_{3',4'} = J_{4',5'}$ 7.3 Hz, H-4′), 5.49 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 5.21 (d, 1H, $J_{3,4}$ 3.0 Hz, H-4), 4.80 (dd, 1H, $J_{1,2}$ 3.8 $J_{2,3}$ 10.0 Hz, H-2), 4.02–4.29 (m, 3H, H-5,5′, 6b), 3.83 (dd, 1H, $J_{2,3}$ 10.0 $J_{3,4}$ 3.0 Hz, H-3), 3.72 (dd, 1H, $J_{5,6a}$ 5.9 $J_{6a,6b}$ 11.0 Hz, H-6a), 3.39 (dd, 1H, $J_{5',6'b}$ 5.6 $J_{6'a,6'b}$ 10.1 Hz, H-6′b), 3.31 (dd, 1H, $J_{5',6'a}$ 5.2 $J_{6'a,6'b}$ 10.1 Hz, H-6′a), 3.20, (s, 2H, H-1′a,b) and 1.84, 1.98, 1.99, 2.02, 2.11 (5s, 15H, 5×$CH_3$). $^{13}$C NMR: δ 170.9, 170.5, 170.2, 170.1, 169.5 (*C*O$CH_3$), 143.6, 143.3, 128.6, 127.8, 127.1, 127.0 (Ar-C), 104.5 (C-2′), 90.1 (C-1), 87.0, 86.8 (*C*$Ph_3$), 78.7 (C-5′), 76.1 (C-3′), 74.9 (C-4′), 70.3, 70.1 (C-3,5), 66.8, 66.2 (C-2,4), 64.0 (C-6), 63.5, 61.4 (C-1′,6′) and 20.7, 20.6, 20.5, 20.4 (CO*C*$H_3$). EI-MS *m/z* (%): 289 [M − $C_{48}H_{43}O_8$]$^+$, 243 (100), 165 (71), 105 (15), 43 (22). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 1059.3779. Found: 1059.3784.

**3,4-Di-*O*-acetyl-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,4,6-tri-*O*-acetyl-3-*O*-benzoyl-α-D-galactopyranoside (3).** Conventional benzoylation of **2** (0.051 g, 0.049 mmol) gave **3** (0.045 g, 80%) as a syrup: $[\alpha]_D$ +48.9° (*c* 0.96, $CHCl_3$); $^1$H NMR: δ 7.12–7.83 (m, 35H, Ar-*H*), 5.76 (d, 1H, $J_{3',4'}$ 7.3 Hz, H-3′), 5.57 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 5.58 (d, 1H, H-4), 5.76 (d, 1H, $J_{3',4'}$ 7.3 Hz), 5.26 (dd, 1H, $J_{2,3}$ 11.0 $J_{3,4}$ 3.1 Hz, H-3), 5.14 (dd, 1H, $J_{1,2}$ 3.8 $J_{2,3}$ 11.0 Hz, H-2), 4.36–4.40 (m, 1H, H-5), 4.05–4.16 (m, 2H, H-5′,6b), 3.80 (dd, 1H, $J_{5,6a}$ 5.9 $J_{6a,6b}$ 11.1 Hz, H-6a), 3.38 (dd, 1H, $J_{5',6'b}$ 5.6 $J_{6'a,6'b}$ 10.4 Hz, H-6′b), 3.28 (dd, 1H, $J_{5',6'a}$ 4.5 $J_{6'a,6'b}$ 10.4 Hz, H-6′a), 3.11, (s, 2H, H-1′a,b), 1.68, 1.79, 1.93, 1.98, 2.00 (5s, 15H, 5×$CH_3$). $^{13}$C NMR: δ 170.2, 170.0, 169.8, 169.7 (*C*O$CH_3$), 165.3 (Ph*C*O), 143.7, 143.4, 128.7,

128.4, 127.9, 127.8, 127.1 (Ar-*C*), 104.3 (C-2′), 89.6 (C-1), 87.1 (*C*Ph$_3$), 78.9 (C-5′), 75.7 (C-3′), 74.6 (C-4′), 68.4, 67.8 (C-3,5), 67.2 (C-2), 66.8 (C-4), 64.0, 63.5, 61.0 (C-1′,6,6′), 20.8, 20.6, 20.5 (CO*C*H$_3$). EI-MS *m/z* (%): 393 [M − $C_{48}H_{43}O_8$]$^+$, 243 (94), 165 (100), 105 (93). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 1163.4023. Found: 1163.4041.

**Methyl 2,4-di-*O*-acetyl-6-*O*-trityl-α-D-galactopyranoside (7).** Treatment of **6** (0.300 g, 0.577 mmol) in dichloromethane (15 mL) with DAST (0.19 mL, 1.45 mmol) as described for **2** gave, after flash column chromatography (ethyl acetate/hexane, 1:1), crystalline **7** (0.215 g, 72%): mp 153–155°C (ethanol); [α]$_D$ +41.2° (*c* 0.98, $CHCl_3$); $^1$H NMR: δ 7.16–7.36 (m, 15H, Ar-*H*), 5.40 (dd, 1H, $J_{3,4}$ 3.5 $J_{4,5}$ 1.0 Hz, H-4), 4.81–4.88 (m, 2H, H-1,2), 4.12–4.15 (m, 1H, H-3), 3.88–3.92 (m, 1H, H-5), 3.32 (s, 3H, $CH_3$), 3.26 (dd, 1H, $J_{5,6b}$ 3.1 $J_{6a,6b}$ 9.4 Hz, H-6b), 3.02 (dd, 1H, $J_{5,6a}$ 7.0 $J_{6a,6b}$ 9.4 Hz, H-6a), 1.87, 2.07 (2s, 6H, 2×$CH_3$). $^{13}$C NMR: δ 171.1, 170.9 (*C*O*C*H$_3$), 143.5, 128.5, 127.8, 127.0 (Ar-*C*), 97.1 (C-1), 86.8 (*C*Ph$_3$), 71.4 (C-3), 70.9 (C-5), 67.6 (C-2), 66.8, (C-4), 61.6 (C-6), 55.3 (O*C*H$_3$) and 20.9, 20.5 (CO*C*H$_3$). EI-MS *m/z* (%): 520 [M$^+$] (<0.5), 489 [M - OCH$_3$]$^+$ (<0.5), 243 (100), 215 (13), 165 (62), 105 (21), 43 (26). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 543.1995. Found: 543.1987.

Anal. Calcd for $C_{30}H_{32}O_8$: C, 69.23; H, 6.15. Found: C, 68.95; H, 6.20.

**Methyl 2,3-di-*O*-acetyl-4-*O*-(*N,N*-diethylaminosulfinyl)-6-*O*-trityl-α-D-glucopyranoside (9a,b).** Compound **(6)** (0.210 g, 0.404 mmol) in dichloromethane (15 mL) was treated with DAST (0.14 mL, 1.07 mmol) at −25°C under argon atmosphere for ∼5 min. The reaction mixture was washed successively with satd $NaHCO_3$ and brine, dried ($Na_2SO_4$) and concentrated under reduced pressure at 0°C. Flash column chromatography (ether/hexane, 3:1) gave first, the sulfinates **9a,b** as a colorless syrup (0.104 g, 40%); [α]$_D$ +55.4° (*c* 0.33, $CHCl_3$); $^1$H NMR: δ 7.14–7.42 (m, 30H, Ar-*H*), 5.39 (t, 1H, $J_{2,3}$ 10.1, $J_{3,4}$ 9.1 Hz, H-3), 5.36 (t, 1H, $J_{2',3'}$ 10.5, $J_{3',4'}$ 10.1 Hz, H-3′), 4.96 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1), 4.93 (d, 1H, $J_{1',2'}$ 3.5 Hz, H-1′), 4.83 (dd, 1H, $J_{1',2'}$ 3.5 $J_{2',3'}$ 10.5 H-2′), 4.74 (dd, 1H, $J_{1,2}$ 3.8 $J_{2,3}$ 10.1 Hz, H-2), 3.72–4.01 (m, 4H, H-4,4′,5,5′), 3.50 (s, 3H, $OCH_3$), 3.50 (s, 3H, $OCH_3$), 3.31–3.34 (m, 2H, H-6a,b), 3.21 (dd, 1H, $J_{5',6'a}$ 7.7, $J_{6'a,6'b}$ 10.0 Hz, H-6′a), 3.10 (dd, 1H, $J_{5',6'b}$ 5.2 $J_{6'a,6'b}$ 10.0 Hz, H-6′b), 2.55–2.86 (m, 8H, 4×$CH_2$), 1.96, 2.01, 2.02, 2.04 (4s, 12H, 4×$COCH_3$), 0.82, 0.84, 0.87, 0.90 (4s, 12H, 4×$CH_3$). $^{13}$C NMR: δ 170.3, 170.2, 169.7 (*C*O*C*H$_3$), 143.8, 143.6, 128.8, 127.6 (Ar-*C*), 96.3, 96.5 (C-1,1′), 86.4 (*C*Ph$_3$), 69.4,69.6, 69.9, 70.7, 71.2, 71.6 (C-2,2′,3,3′,4,4′,5,5′), 62.1, 63.1 (C-6,6′), 54.9, 55.0 (O*C*H$_3$), 35.8, 35.9 (*C*H$_2$), 20.7, 20.9, 21.7 (CO*C*H$_3$), 13.5, 13.6 (*C*H$_3$). EI-MS *m/z* (%): 520 [M − $C_4H_{10}NSO$]$^+$ (<0.5), 488 [M − $C_5H_{13}NSO_2$]$^+$ (<0.5), 433 (20), 301 (12), 243 (100), 215 (21), 165 (68), 105 (36), 43 (43).

Anal. Calcd For $C_{34}H_{41}NSO_9$: C, 63.85; H, 6.42; N, 2.19; S, 5.01. Found: C, 63.55; H, 6.40; N, 2.23; S, 4.88.

Eluted second is the recovered starting material, **6** (0.042 g, 20%).

Eluted last is the migrated product, **7** (0.051 g, 24%).





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**Methyl 2,4-di-*O*-acetyl-3-*O*-benzoyl-6-*O*-trityl-α-D-galactopyranoside (8).** Compound **7** (0.092 g, 0.177 mmol) was benzoylated to give **8** (0.095 g, 86%): mp 195–197°C (ethanol); $[\alpha]_D$ +62.6° (*c* 0.82, $CHCl_3$); $^1H$ NMR: δ 7.16–7.85 (m, 20H, Ar-*H*), 5.61 (d, 1H, $J_{3,4}$ 3.1 Hz, H-4), 5.52 (dd, 1H, $J_{2,3}$ 10.8 $J_{3,4}$ 3.1 Hz, H-3), 5.26 (dd, 1H, $J_{1,2}$ 3.5 $J_{2,3}$ 10.8 Hz, H-2), 4.89 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 3.37 (s, 3H, $OCH_3$), 4.03–4.08 (m, 1H, H-5), 3.27 (dd, 1H, $J_{5,6b}$ 6.3 $J_{6a,6b}$ 9.4 Hz, H-6b), 3.04 (dd, 1H, $J_{5,6a}$ 7.0 $J_{6a,6b}$ 9.4 Hz, H-6a), 1.82, 1.94 (2s, 6H, 2×$CH_3$). $^{13}C$ NMR: δ 170.4, 169.5 (*C*$OCH_3$), 165.3 (Ph*C*O), 143.5, 133.1, 129.5, 127.1 (Ar-*C*), 97.3 (C-1), 86.9 (*C*$Ph_3$), 68.6, 68.5, 68.3, (C-2,3,5), 67.7 (C-4), 61.6 (C-6), 55.4 (O*C*$H_3$) and 20.7, 20.4 (CO*C*$H_3$). EI-MS *m/z* (%): 592 $[M - OCH_3]^+$ (<0.5), 243 (100), 165 (67), 127 (20), 105 (88), 43 (34). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 647.2257. Found: 647.2252.

Anal.Calcd for $C_{37}H_{36}O_9$: C, 71.13; H, 5.83. Found: C, 71.08; H, 5.74.

**2,4-Di-*O*-acetyl-6-*O*-trityl-α-D-galactopyranosyl 2,4-di-*O*-acetyl-6-*O*-trityl-α-D-galactopyranoside (15).** A solution of 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranosyl 2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (**13**) (0.171 g, 0.172 mmol) in dichloromethane (10 mL) was treated with DAST as for **2** for ~2 1/2 h. Work-up in the usual way followed by flash column chromatography (ether/hexane, 9:1) gave **15** as a white solid (0.132 g, 77%): mp 150–152°C; $[\alpha]_D$ +31.1° (*c* 0.64, $CHCl_3$); $^1H$ NMR: δ 7.16–7.28 (m, 30H, Ar-*H*), 5.49 (d, 2H, $J_{3,4} = J_{3',4'}$ 2.4 Hz, H-4,4′), 5.26 (d, 2H, $J_{1,2} = J_{1',2'}$ 3.8 Hz, H-1, 1′), 5.06 (dd, 2H, $J_{1,2} = J_{1',2'}$ 3.8 $J_{2,3} = J_{2',3'}$ 10.4 Hz, H-2, 2′), 4.25–4.32 (m, 4H, H-3,3′,5,5′), 2.94–3.19 (m, 4H, H-6a,b, H-6′a,b), 1.86, 1.94 (2s, 12H, 4×$CH_3$). $^{13}C$ NMR: δ 171.1, 170.8 (*C*$OCH_3$), 143.2, 128.5, 127.8, 127.2 (Ar-*C*), 92.3 (C-1,1′), 86.7 (*C*$Ph_3$), 71.1 (C-5,5′), 70.5 (C-3,3′), 69.1 (C-2,2′), 67.4, (C-4,4′), 61.4 (C-6,6′) and 21.0, 20.9 (CO*C*$H_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1017.3657. Found: 1017.3687

Anal. Calcd for $C_{58}H_{58}O_{15}$: C, 70.02; H, 5.83. Found: C, 69.69; H, 5.79.

Conventional benzoylation of **15** (0.083 g, 0.0835 mmol) gave **17** as a white solid (0.084 g, 84%): mp 138–140°C (ethanol); $[\alpha]_D$ +87.6° (*c* 1.09, $CHCl_3$); $^1H$ NMR: δ 7.10–7.88 (m, 40H, Ar-*H*), 5.73 (d, 2H, $J_{3,4} = J_{3',4'}$ 2.8 Hz, H-4,4′), 5.61 (dd, 2H, $J_{2,3} = J_{2',3'}$ 10.8 $J_{3,4} = J_{3',4'}$ 2.8 Hz, H-3, 3′), 5.56 (dd, 2H, $J_{1,2} = J_{1',2'}$ 3.1 $J_{2,3} = J_{2',3'}$ 10.8 Hz, H-2, 2′), 5.39 (d, 2H, $J_{1,2} = J_{1',2'}$ 3.1 Hz, H-1, 1′), 4.45–4.49 (m, 2H, H-5,5′), 2.95–3.20 (m, 4H, H-6a,b, H-6′a,b), 1.81, 1.89 (2s, 12H, 4×$CH_3$). $^{13}C$ NMR: δ 170.1, 169.6 (*C*$OCH_3$), 165.3 (Ph*C*O), 143.2, 133.3, 129.6, 128.5, 127.9, 127.1 (Ar-*C*), 92.5 (C-1, 1′), 86.8 (*C*$Ph_3$), 69.2, 69.0, 68.6 (C-2,2′,3,3′5,5′), 66.9 (C-4,4′), 61.6 (C-6,6′), and 20.9, 20.4 (CO*C*$H_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1125.4179. Found: 1225.4213.

Anal.Calcd for $C_{72}H_{66}O_{17}$: C, 71.93; H, 5.53. Found: C, 72.01; H, 5.71.

When the above reaction was interrupted after about 30 min, TLC (ether) showed traces of a fast (which appears to be the diastereomeric sulfinates but the quantity is too small to be isolated and characterised) and two slower moving compounds. Work-up in the usual way followed by flash chromatography (ether) gave

first the asymmetric derivative **19** (45%) mp 118–120°C (ether-hexane); $[\alpha]_D$ +53.0° (*c* 1.53, $CHCl_3$); $^1H$ NMR: δ 7.17–7.35 (m, 30H, Ar-H), 5.48 (d, 1H, $J_{3,4}$ 3.0 Hz, H-4), 5.23–5.34 (m, 3H, H-1,1′,3′), 4.97–5.04 (m, 2H, H-2,2′), 4.34 (dd, 1H, $J_{2,3} = J_{3,4}$ 3.0 $J_{3,OH}$ 10.4 Hz, H-3), 4.25–4.29 (m, 1H, H-5), 3.88–3.94 (m, 1H, H-5′), 3.69 (t, 1H, $J_{3',4'} = J_{4',5'}$ 9.4 Hz, H-4′), 2.93–3.31 (m, 4H, H-6a,b, H-6′a,b), 1.85, 1.88, 1.91, 2.03 (4s, 12H, 4×$CH_3$). $^{13}C$ NMR: δ 171.4, 171.0, 170.4, 169.8 (*C*O$CH_3$), 143.4, 143.2, 128.5, 127.9, 127.8, 127.1 (Ar-*C*), 92.5, 92.2 (C-1,1′), 86.9, 86.7 (*C*$Ph_3$), 73.0 (C-3), 71.1, 71.0 (C-5,5′), 70.4, 70.3, 69.9, 69.1, 66.9 (C-2,2′,3′,4,4′), 63.1, 61.5 (C-6,6′), and 20.9, 20.7, 20.6 (CO*C*$H_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1017.3673. Found: 1017.3682.

Anal. Calcd for $C_{58}H_{58}O_{15}$: C, 70.02; H, 5.83. Found: C, 69.89; H, 6.05.

Eluted second is **15** (25%).

**2,4-Di-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranosyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (16).** Treatment of **14** (0.497 g, 0.597 mmol) in dichloromethane (20 mL) with DAST (0.20 mL, 1.53 mmol) as described for **2** gave, after flash column chromatography (ethyl acetate/hexane, 11:9), **16** (0.390 g, 78%) as a white solid: mp 96–98°C (ether-hexane); $[\alpha]_D$ +96.5° (*c* 0.51, $CHCl_3$); $^1H$ NMR: δ 7.19–7.51 (m, 10H, Ar-*H*), 5.52 (d, 1H, $J_{3,4}$ 2.8 Hz, H-4), 5.43 (t, 1H, $J_{2',3'} = J_{3',4'}$ 10.0 Hz, H-3′), 5.18 (d, 2H, $J_{1,2} = J_{1',2'}$ 3.8 Hz, H-1,1′), 4.95–5.02 (m, 3H, H-2,2′,4′), 4.32–4.36 (m, 1H, H-3), 3.54–4.20 (m, 6H, H-5,5′,6a,b,6′a,b), 1.88, 1.91, 1.96, 1.98, 2.02, 2.06 (s, 18H, 6×$CH_3$), 0.96 (s, 9H, C(C*H*$_3$)$_3$). $^{13}C$ NMR: δ 171.1, 170.5, 170.4, 170.1, 169.4, 169.3 (*C*O$CH_3$), 135.5, 135.4, 132.5, 129.8, 127.7 (Ar-*C*), 92.7, 91.9 (C-1,1′), 70.5 (C-3), 70.2, 70.1 (C-5,5′), 69.9, 69.8 (C-2,2′), 68.4, 68.0 (C-4,4′), 66.8 (C-,3′), 61.7, 61.2 (C-6,6′), 26.7 [C(*C*$H_3$)$_3$], 20.7, 20.6, 20.5, 20.4 (CO*C*$H_3$) and 18.9 [*C*($CH_3$)$_3$]. EI-MS *m/z* (%): 485 $[M - C_{14}H_{19}O_{10}]^+$ (5), 365 (18), 331 $[M - C_{26}H_{33}O_8Si]^+$ (60), 241 (84), 199 (82), 169 (100), 109 (66), 43 (80). HRMS-ESI (positive mode): calcd for $[M + Na]^+$. 855.2856. Found: 855.2863.

Anal. Calcd for $C_{40}H_{52}O_{17}Si$: C, 57.69; H, 6.25. Found: C, 57.78; H, 6.18.

Benzoylation of **16** (0.117 g, 0.140 mmol) in the conventional manner gave **18** (0.108 g, 82%): mp 78–80°C (ethanol); $[\alpha]_D$ +116.2° (*c* 0.88, $CHCl_3$); $^1H$ NMR: δ 7.27–8.05 (m, 15H, Ar-*H*), 5.78 (d, 1H, $J_{3,4}$ 3.0 Hz, H-4), 5.59 (dd, 1H, $J_{2,3}$ 10.8 $J_{3,4}$ 3.0 Hz, H-3), 5.39–5.48 (m, 2H, H-2,3′), 5.23–5.25 (m, 2H, H-1,1′), 4.96–5.04 (m, 2H, H-2′,4′), 3.93–4.28 (m, 4H, H-5,5′,6′a,b), 3.55–3.57 (m, 2H, H-6a,b), 1.84, 1.96, 1.97, 1.97, 1.98, 2.01 (6s, 18H, 6×$CH_3$), 0.96 (s, 9H, C($CH_3$)$_3$). $^{13}C$ NMR: δ 170.4, 169.8, 169.7, 169.5, 169.4 (*C*O$CH_3$), 165.1 (Ph*C*O), 135.5 - 127.7 (Ar-C), 92.8, 92.0 (C-1,1′), 70.0, 69.6, 69.5, 68.4, 68.3, 67.9, 67.5, 67.2 (C-2,2′,3,3′,4,4′,5,5′), 61.6, 60.9 (C-6,6′), 26.5 [C(*C*$H_3$)$_3$], 20.4, 20.2 (CO*C*$H_3$) and 18.8 [*C*($CH_3$)$_3$]. EI-MS *m/z* (%): 589 $[M - C_{14}H_{19}O_{10}]^+$ (6), 365 (19), 331 $[M - C_{33}H_{37}O_9Si]^+$ (48), 241 (67), 199 (71), 169 (100), 109 (35), 105 (86), 43 (18). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 959.3134. Found: 959.3138.

Anal. Calcd for $C_{47}H_{56}O_{18}Si$: C, 60.27; H, 5.98. Found: C, 60.03; H, 6.01.

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