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REGIOSELECTIVE STANNYLATION

ACYLATION OF CARBOHYDRATES[1]: COORDINATION CONTROL

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Abstract—An efficient method for the regioselective enhancement of the nucleophilicity of polyhydroxy compounds has been developed. Partial stannylation of carbohydrate with $(Bu_3Su)_2O$ and subsequent electrophilic attack with benzoyl chloride gave rise to regioselectively benzoylated product.

Selective acylation of carbohydrates has been thoroughly studied employing a variety of acylating reagents.[2] The accumulated results have been used for the transformation of simple carbohydrates into molecules of biological importance, such as antibiotics, oligosaccharides, and non-carbohydrate natural products.

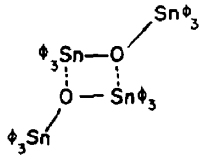
In 1974, in order to complement the available methodologies for the selective acylation and alkylation of OH groups, Moffatt *et al.*[3] introduced the use of dibutylstannylidene derivatives for the selective activation of a *vic*-diol system in the field of nucleosides, and this approach has been successfully applied to carbohydrate derivatives.[4] As part of our project[5] on the chemical transformation of carbohydrates through trialkylstannylation,[6] we now describe regioselective stannylation and subsequent acylation of carbohydrates.

Trialkyltin alkoxide is more nucleophilic than the original OH group[7] and forms a coordination bond with a neighbouring O atom at the Sn atom[8] such as **1** and **2**. Therefore intramolecular coordination as depicted in **4** could be expected to occur when one equivalent of stannylating reagent $(Bu_3Sn)_2O$ is employed for the reaction with **3**. Subsequent reaction of **4** with electrophile should lead to the isolation of the regioselectively modified product **5**.

In fact, triol **6** was first stannylated with one equivalent of $(Bu_3Sn)_2O$ and subsequent treatment with benzoyl chloride gave monobenzoate **8** in 67% yield. The structure of **8** was confirmed by ^1H NMR data which showed one proton quartet at δ 4.38 with $J_{12} = 4Hz$ and $J_{1'1} =$ 11Hz for H-1 and one proton doublet at δ 4.19 with $J_{1'1} = 11Ha$ for H-1'.

Cyclohexane - *cis* - 1,2 - diol forms an O - isopropylidene derivatives more readily than cyclohexane - *trans* - 1,2 - diol[9] and similarly the formation of cyclic kelal **9** from *cis*-vicinal diol on a pyranose ring is much easier than the formation of **10** from *trans*-vicinal diol[10]. By analogy with this, the formation of five membered coordination ring **11** from *cis*-vicinal diol was expected to be much favored than the formation of **12** from *trans*-vicinal diol.

According to this speculation, stannylation of methyl α-D-glucopyranoside **13** with two equivs of $(Bu_3Sn)_2O$ should give rise to the regioselectively stannylated product **14**. Actually, stannylation[11] of **13** with 3 equivs of $(Bu_3Sn)_2O$ and subsequent treatment of the presumed



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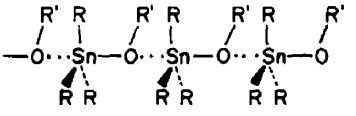

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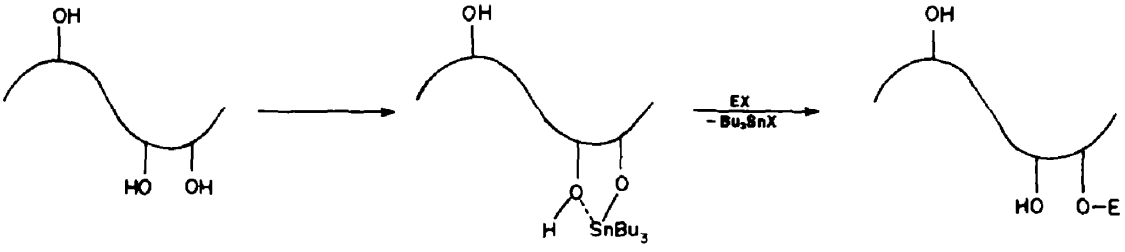

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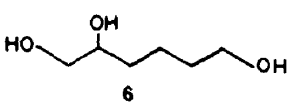

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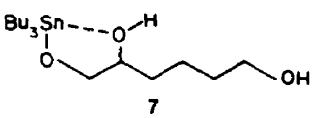

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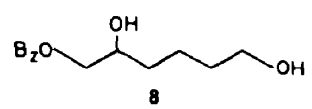

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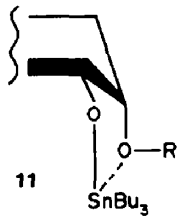
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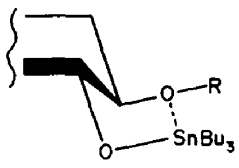
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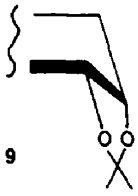
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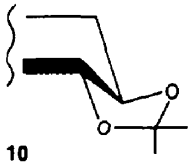
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intermediate **14** with BzCl for 7 hr at 20° afforded an 81.4% yield of methyl 2,6 - di - 0 - benzoyl - α - D - glucopyranoside **15** and an 18.4% yield of methyl 2,3,6 - tri - 0 - benzoyl - α - D - glucopyranoside **16**. The structure of dibenzoate **15** and tribenzoate **16** was confirmed by ^{1}H NMR data (Experimental). The observed high regioselectivity of benzoylation strongly indicate the intermediacy of the 2,6 - di - 0 - stannyl derivative **14** in the above transformation of **13** into **15**. The same dibenzoate **15** had been prepared in 1935 by Lieser and Schweizer[12] in 50% yield from **13** using benzoyl chloride and pyridine and the structure was confirmed by ^{1}H NMR data by Williams and Richandson.[13] The overall yield of **15** from **13** via **14** could be improved by performing the benzoylation at lower temperature. When benzoylation of **14** was performed for 20 hr at $-10° \sim -5°$, essentially a quantitiative yield of dibenzoate **15** could be obtained. In addition, when the reaction was intercepted after 1.5 hr at $-10°$ with the addition of acetic acid, a 73% yield of 6-benzoate **17** was isolated along with a 20% yield of dibenzoate **15**. This indicate higher reactivity of the primary tributyltin ether than the secondary one in **14** toward benzoyl chloride. Employing large excess of $(Bu_3Sn)_2O$ and BzCl, tribenzoate **16** became a major product of the reaction, but methyl 2,3,4,6 - tetra - 0 - benzoyl - α - D - glucopyranoside **18** was not isolated by this procedure presumably due to the difficulty to stannylate the OH group at C-4. Thus stannylation of **13** with five equivs of $(Bu_3Sn)_2O$ and subsequent treatment with excess of BzCl for 4 days at 50° gave a 63% yield of tribenzoate **16**.

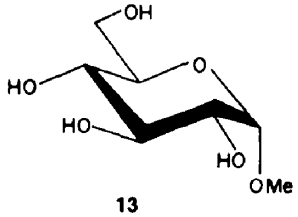
Next, we examined the reactivity of **14** toward sulfonyl chloride. Treatment of **14** with tosyl chloride for 3 days at 20° gave rise to the mixture of 2,6-ditosylate **19** (15.9%), 2-tosylate **20** (40.5%) and 6-tosylate **21** (36.4%). Continuation of the above reaction for a further 4 days at 50° led to the isolation of di-tosylate **19** in 80.6% yield. In the same manner, 2,6-dimesylate **22** was obtained in 75.4% yield from **13**. The structure of tosylates **19**, **20** and **21** was confirmed by ^{1}H NMR data. The synthesis of ditosylate **19** in 20% and monotosylate **21** in 5% yield was first reported in 1955 by Asselineau.[14] And in 1963 Jary[15] *et al.* improved the yield of ditosylate **19** up to 69% using tosyl chloride and pyridine. The synthesis of dimesylate **22** from **13** in 57% yield had been reported by Mitra *et al.*[16] in 1962.

Next, methyl β - D - galactopyranoside **23** was chosen as the substrate for stannylation. The OH group at C-3 has a *cis* axial neighbouring O function at C-4, therefore partially stannylated structure is expected to be the coordination controlled product **24**, giving rise to the formation of 3,6-dibenzoate **25** upon treatment with benzoyl chloride. As a matter of fact, treatment of **23** with three equivs of $(Bu_3Sn)_2O$ and subsequent reaction of **24** with benzoyl chloride for 5 hr at 20–25° led to the isolation of dibenzoate **25** and 2,3,6-tribenzoate **26** in 95 and 4.7% yield respectively. The structure of **25** and **26** was determined by ^{1}H and ^{13}C NMR data shown in Experimental.

It is to be noted that the preferred reactivity of C-3 OH group over C-2 in **23** was previously reported by Chalk *et al.*[17] in 1966. Thus, dimolar mesylation of **23** with mesyl chloride–pyridine afforded methyl 3,6 - di - 0 - mesyl - β - D - galactopyranoside in 26% yield. Compared to this, stannylation–acylation sequence on **23** did enhance the nucleophilicity of C-3 OH group with high selectivity from the preparative view point.

In the case of methyl α - D - galactopyranoside **27**, partial stannylation is expected to give two isomers **28** and **29**, therefore no regioselectivity for dimolar benzoylation should be observed. As expected, stannylation and subsequent benzoylation of **27** gave rise to the mixture of 2,3,6-tribenzoate **30**[18] (40%), 2,6 - di - benzoate **31** (10%), 3,6 - di - benzoate **32** (20%), and 6 - benzoate **33** (22%). Direct benzoylation of **27** with benzoyl chloride in pyridine was reported by Williams and Richardson[13] in 1967 to give also a mixture of **30**[18], **32** and two other products.

Above experiments employing methyl α- and β - D - galactopyranoside proved the crucial importance of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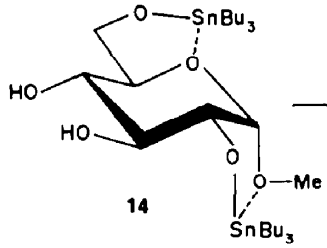
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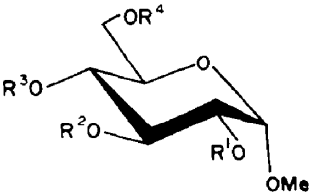
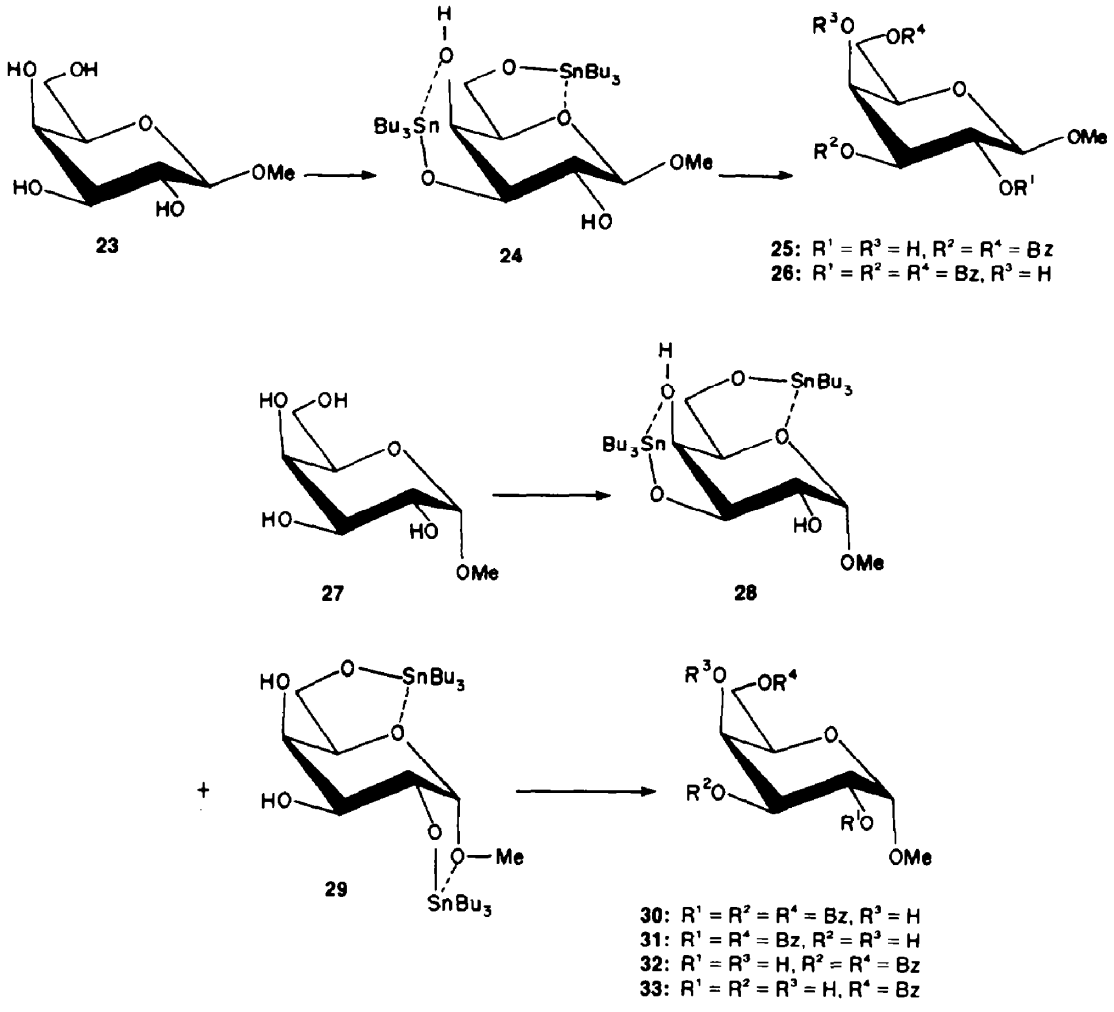


15: $R^1 = R^4 = Bz$, $R^2 = R^3 = H$
16: $R^1 = R^2 = R^4 = Bz$, $R^3 = H$
17: $R^1 = R^2 = R^3 = H$, $R^4 = Bz$
18: $R^1 = R^2 = R^3 = R^4 = Bz$
19: $R^1 = R^4 = Ts$, $R^2 = R^3 = H$
20: $R^1 = Ts$, $R^2 = R^3 = R^4 = H$.
21: $R^1 = R^2 = R^3 = H$, $R^4 = Ts$
22: $R^1 = R^4 = Ms$, $R^2 = R^3 = H$

anomeric configuration in order to attain the high reactivity at OH group at C-3 in galactopyranosyl moiety by stannylation–acylation sequence.

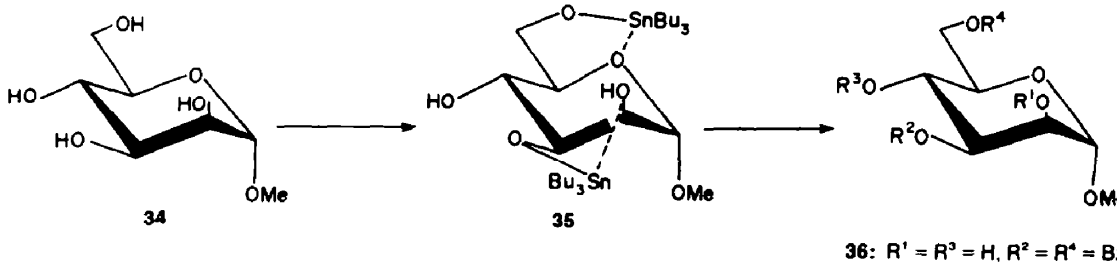


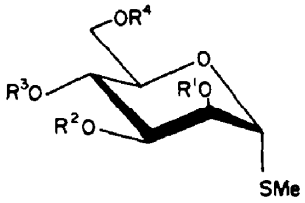
Stannylation and subsequent benzoylation of methyl α - D - mannopyranoside afforded 3,6 - dibenzoate **36** in 90% yield through the intermediacy of coordination controlled product **35**. The same dibenzoate had been prepared by Williams and Richardson[13] in 62% yield from **34** with pyridine–benzoyl chloride.

Similar high regioselectivity of acylation was observed according to this approach employing thioglycosides such as **37** and **41** as substrates.

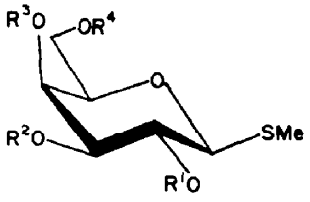
Methyl 1 - deoxy - 1 - thio - α - D - mannopyranoside[19] **37** was stannylated with 3 equivs of $(Bu_3Sn)_2O$ and subsequently treated with benzoyl chloride to afford 3,6-dibenzoate **39** and 2,3,6-tribenzoate **40** in 66.4 and 12.0% yields respectively. Starting from methyl 1 - deoxy - 1 - thio - β - D galactopyranoside **41**,[21] a similar sequence of reactions afforded 3,6-dibenzoate **43** and 2,3,6,-tribenzoate **44** in 95.7 and 2.7% yields respectively. The observed high regioselectivity in obtaining **39** and **43** should be explained in terms of the intermediacy of the partially stannylated structures **38** and **42** respectively.

The applicability of the stannylation–acylation procedure was further examined using typical disaccharides, sucrose **45** and αα-trehalose **47**. Stannylation of sucrose **45** with 6 equivs of $(Bu_3Sn)_2O$, followed by benzoylation with benzoyl–chloride led to the isolation





37: $R^1 = R^2 = R^3 = R^4 = H$
38: $R^1 = R^3 = H, R^2 = R^4 = SnBu_3$
39: $R^1 = R^3 = H, R^2 = R^4 = Bz$
40: $R^1 = R^2 = R^4 = Bz, R^3 = H$

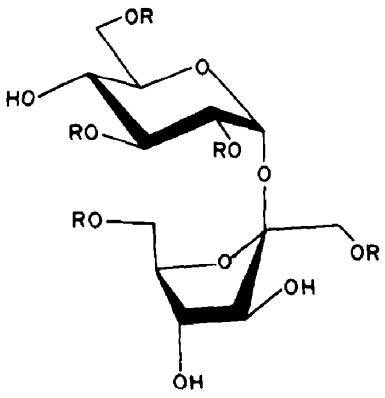


41: $R^1 = R^2 = R^3 = R^4 = H$
42: $R^1 = R^3 = H, R^2 = R^4 = SnBu_3$
43: $R^1 = R^3 = H, R^2 = R^4 = Bz$
44: $R^1 = R^2 = R^4 = Bz, R^3 = H$

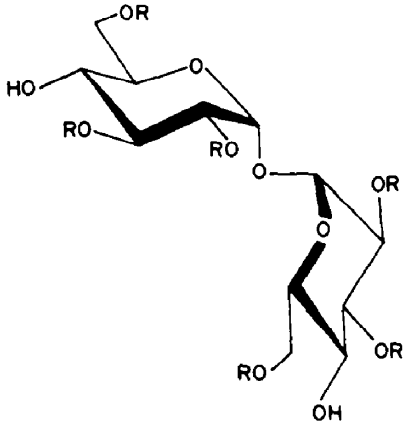
of an 87% yield of 2,3,6,1′,6′ - pentabenzoate **46**. The structure was deduced from ^1H and ^{13}C NMR data. ^1H NMR spectrum of **46** revealed a deshielded triplet for H-3 at δ 6.01 with $J_{23} = J_{34} = 10Hz$, and a deshielded quartet for H-2 at δ 5.33 with $J_{12} = 4Hz$ and $J_{23} = 10Hz$, in agreement with the assigned structure. ^{13}C NMR of **46** disclosed three deshielded signals[22] for three primary benzoyloxy carbons at δ 65.3, 64.2 and 63.8, confirmining that three primary alcohols were all benzoylated.

In the case of $\alpha\alpha$-trehalose, stannylation with 6 equivs of $(Bu_3Sn)_2O$ and subsequent benzoylation gave rise to the isolation of 2,3,6,2′,3′,6′ - hexabenzoate **48** in 73.1% yield. The structure of **48** was assigned from ^1H NMR data which showed a deshielded triplet for H-3 and H-3′ at δ 5.91 with J = 10Hz and a deshielded quartet for H-2 and H-2′ at δ 5.43 with J = 4 and 10Hz.

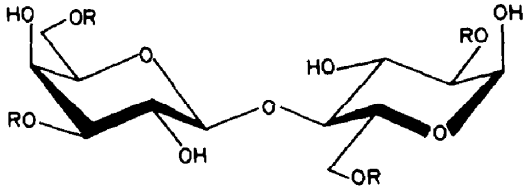
Finally, free lactose **49** was submitted to the reaction. Stannylation and subsequent benzoylation led to the



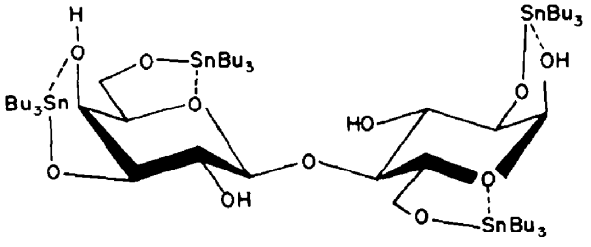
45: R = H
46: R = Bz



47: R = H
48: R = Bz



49: R = H
51: R = Bz



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isolation of a 72% yield of 2,6,3',6' - tetrabenzoate **51** presumably through the intermediacy of **50**. Even though ^{1}H NMR of **51** was not informative, the structure of **51** could be assigned from ^{13}C NMR which showed four signals at δ 72.8(C-2), 63.6(C-6), 76.2(C-3') and 63.9(C-6') in lower field compared to the corresponding signals of α-lactose in the amount of +1.5, +3.2, +2.9 and +3.0 ppm respectively due to the α effect of benzoylation.[22] And β-was observed only for C-1 (− 1.7 ppm) and not for C-1' (− 0.1 ppm), confirming the location of secondary benzoates at O-2 and O-3'.

In conclusion, an efficient and practical procedure for the regioselective enhancement of the nucleophilicity of OH groups of carbohydrates can be achieved through the intermediacy of partially stannylated derivatives stabilized by intramolecular coordination. According to this approach several partially benzoylated mono- and disaccharides of high synthetic potential have been prepared in good to high yields.

EXPERIMENTAL

M.ps were determined with a Yanagimoto micro melting point apparatus and were uncorrected. Optical rotations were determined with a Parkin–Elmer Model 141 polarimeter for solns in $CHCl_3$ at 25°, unless otherwise noted. IR spectra were recorded with an EPI-G2 Hitachi spectrophotometer, as KBr discs for the crystalline samples and as neat films for the liquid samples. ^{1}H-NMR spectra were recorded with a Varian HA-100 NMR spectrometer, with TMS as an internal standard. ^{13}C NMR spectra were recorded with a JNM-FX 100FT NMR spectrometer at 25.05 MHz. The values of δ_C and δ_H are expressed in ppm downward from the internal standard for the solns in $CDCl_3$ unless otherwise noted. Column chromatography was performed on columns of Silica Gel Merck (70-230 mesh; E. Merck, Darmstadt, West Germany). Tlc was performed on precoated plates (layer thickness, 0.25 mm; E. Merck, Darmstadt, West Germany) of Silica Gel $60F_{254}$.

1-Benzoyloxy-2,6-di-hydroxy-n-hexane **8**

A mixture of **6** (1.34 g, 10 mmol) and $(Bu_3Sn)_2O$ (3.0 g, 5 mmol) was refluxed in toluene (50 ml) for 4 hr at 140° with continuous azeotropic removal of water. To a cooled soln was added dropwise BzCl (1.4 g, 10 mmol) during 5 min at 0°. The mixture was stirred for 2 hr at 0° and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (100 g, toluene–EtOAc, 1:3) to give **8** (1.127 g, 47%; 67% based on the consumed triol); R_f 0.25 in toluene–EtOAc (1:3). NMR δ_H: 8.04(2H, dd, J = 8, 2Hz, benzoyl), 7.64–7.32(3H, m, benzoyl), 4.38 (1H, dd, J = 4, 11Hz, H-1), 4.19(1H, d, J = 11Hz, H-1'), 3.98(1H, m, H-2) and 3.64(2H, m, H-6, H-6'). Further elution with CH_2Cl–MeOH (5:1) gave starting triol **6** (465 mg, 34.7%).

Methyl 2,6 - di - 0 - benzoyl - α - D - glucopyranoside **15** *and methyl 2,3,6 - tri - 0 - benzoyl - α - D - glucopyranoside* **16**

(A) Compound **13** (485 mg, 2.5 mmol) was stannylated with $(Bu_3Sn)_2O$ (2.25 g, 3.75 mmol) in toluene (25 ml). To the cooled soln was added BzCl (1.05 g, 7.5 mmol) at 20°. The mixture was stirred for 7 hr at 20° and then was concentrated *in vacuo*. The residue was submitted to chromatography on SiO_2 (100 g, toluene–EtOAc 1:1) to afford **16** (233 mg, 18.4%). Crystals from i-Pr_2O–pentane, m.p. 127–129°. $[\alpha]_D$ + 149.4° (*c* = 0.49), R_f 0.75 in toluene–EtOAc (1:1). NMR δ_H: 5.78(1H, t, J = 9 Hz, H-3), 5.24(1H, dd, J = 4, 12 Hz, H-2), 5.13(1H, d, J = 4 Hz, H-1), 4.80(1H, dd, J = 4, 12 Hz, H-6), 4.61(1 H, dd, J = 2, 12 Hz, H-6'), 4.08(1H, m, H-5), 3.86(1H, t, J = 10 Hz, H-4), 3.43(3H, s, OMe). (Found: C, 66.28; H, 5.20. $C_{28}H_{26}O_9$ requires: C, 66.39; H, 5.17%). Further elution with the same solvent afforded **15** (863 mg, 81.4%). Crystals from i-Pr_2O, m.p. 140–142°. $[\alpha]_D$ + 66.1° (*c* = 0.62). NMR δ_H: 5.06(1H, d, J = 4 Hz, H-1), 4.95(1H, dd, J = 4, 10 Hz, H-2), 4.82 (1 H, dd, J = 4, 13 Hz, H-6), 4.53 (1 H, dd, J = 2, 12 Hz, H-6'), 4.19(1 H, t, J = 9 Hz, H-3), 3.97(1 H, m, H_5), 3.59(1 H, t, J = 9 Hz, H-4), 3.40(3 H, s, OMe). δ_C: 97.4 ($^1J_{CH}$ = 172.1 Hz, C-1, − 3.2[a]), 73.9(C-2, + 1.2[a]), 71.8(C-3, − 2.9[a]), 71.0(C-4, − 0.2[a]), 69.6(C-5, − 3.4[a]), 63.8(C-6, + 1.6[a]), 55.3(OMe). (Found: C, 62.59; H, 5.48. $C_{21}H_{22}O_8$ requires: C, 62.68; H, 5.51%).

(B) Compound **13** (283 mg, 1.46 mmol) was stannylated with $(Bu_3Sn)_2O$ (1.3 g, 2.19 mmol) in toluene (23 ml). To the cooled soln was added dropwise a soln of BzCl (600 mg, 4.4 mmol) in toluene (5 ml) during 5 min at − 10°. The mixture was stirred for 4 hr at − 10° and then left for 17 hr at − 5°. AcOH (0.2 ml) was added and the solvent was evaporated *in vacuo* to give an oily residue which was triturated with i-Pr_2O affording crystalline **15** (588 mg, 95%).

(C) Methyl α-D-glucopyranoside (980 mg, 5 mmol) was stannylated with $(Bu_3Sn)_2O$ (7.5 g, 12.5 mmol) in refluxing toluene. To the cooled soln was added BzCl (3.5 g, 25 mmol) and the mixture was stirred for 4 days at 50°. Usual work-up and chromatography (SiO_2, 100 g, toluene–EtOAc, 10:1) gave **16** (1.6 g, 63%).

Methyl 6-0-benzoyl-α-D-glucopyranoside **17**

Compound **13** (970 mg, 5 mmol) was stannylated with $(Bu_3Sn)_2O$ (4.5 g, 7.5 mmol) in toluene (50 ml) for 2 hr at 140°. To the cooled soln was added dropwise a soln of BzCl (2.1 g, 15 mmol) in toluene (10 ml) during 15 min at − 15° and the mixture was stirred for 1.5 hr at − 10°. AcOH (ml) was added to the mixture and evaporation of the solvent *in vacuo* gave a residual oil which was chromatographed over SiO_2 (100 g, $CHCl_3$–MeOH, 20:1) giving **15** (410 mg, 20.0%) and **17** (1.10 g, 73%); R_f 0.25 in CH_2Cl_2–MeOH (10:1). $[\alpha]_D$ + 91.0° (*c* = 0.50). NMR δ_H: 7.97(2H, dd, J = 2, 8 Hz, benzoyl), 3.36(3H, s, OMe). (Found: C, 55.99; H, 6.02. $C_{14}H_{18}O_7$ requires: C, 56.37; H, 6.08%).

Methyl 2,6 - di - 0 - tosyl - α - D - glucopyranoside **19**, *methyl 6 - 0 - tosyl - α - D - glucopyranoside* **20**, *and methyl 2 - 0 - tosyl - α - D - glucopyranoside* **21**

Compound **13** (0.970 g, 5 mmol) was stannylated with $(Bu_3Sn)_2O$ (4.5 g, 7.5 mmol) in toluene (50 ml). To the resulting toluene soln was added TsCl (2.9 g, 15 mmol) at 20° and the mixture was stirred for 3 days at 20°.

(A) A half of the volume of the mixture was taken in a different flask and was evaporated *in vacuo*. The residue was chromatographed on SiO_2 (100 g, toluene–EtOAc, 1:1) to afford **19** (200 mg, 15.9%) as an oil. $[\alpha]_D$ + 55.7° (*c* = 0.465). R_f 0.5 in toluene–EtOAc (1:1). NMR δ_H: 4.62(1H, d, J = 4 Hz, H-1), 4.34 – 4.08(3H, m, H-6, H-6', and H-2), 3.88(1H, t, J = 9 Hz, H-3), 3.43(1H, t, J = 9 Hz, H-4), 3.22(3H, s, OMe), 2.43(6H, s, aromatic Me × 2). δ_C: 97.1($^1J_{CH}$ = 170.9 Hz, C-1, − 3.5[b]), 78.9(C-2, + 6.2), 69.7(C-3, − 5.0[b]), 70.9(C-4, − 0.3[b]), 68.8(C-5, − 4.2[b]), 68.8(C-6, + 6.8[b]), 55.5 (OMe), 21.6(aromatic Me × 2). (Found: C, 49.90; H, 5.26; S, 12.44. $C_{21}H_{26}O_{10}S_2$ requires: C, 50.19; H, 5.22; S, 12.76%). Further elution with EtOAc–toluene–MeOH (10:1:1) gave **20** (352 mg, 40.5%) as crystals, m.p. 138–139°. $[\alpha]_D$ + 88.6° (MeOH, *c* = 0.56), R_f 0.5 in EtOAc–toluene–MeOH (10:1:1). NMR δ_H (CD_3COCD_3–D_2O):4.66(1H, d, J = 4 Hz, H-1), 4.17(1H, dd, J = 4, 10 Hz, H-2), 3.23(3H, s, OMe), 2.45(3H, s, aromatic Me). (Found: C, 48.59; H, 5.80; S, 9.04. $C_{14}H_{20}O_8S$ requires: C, 48.27; H, 5.79; S, 9.19%). Further elution with the same solvent afforded **21** (317 mg, 36.4%) as crystals, m.p. 103–104°. $[\alpha]_D$ + 102.5° (MeOH, *c* = 0.365), R_f 0.31 in EtOAc–toluene–MeOH (10:1:1). NMR δ_H (CD_3COCD_3–D_2O): 4.54(1H, d, J = 4 Hz, H-1), 4.37(1 H, dd, J = 2, 11 Hz, H-6), 4.18(1 H, dd, J = 6, 11 Hz, H-6'), 3.28(3H, s, OMe), 2.44(3H, s, aromatic Me). (Found: C, 48.16; H, 5.74; S, 8.98. $C_{14}H_{20}O_8S$ requires: C, 48.27; H, 5.79; S, 9.19%).

(B) The remaining half of the mixture was further stirred for 4 days at 50°. The same work-up as above and chromatography over SiO_2 (100 g, toluene–EtOAc, 1:1) afforded **19** (1.013 g, 80.6%) as an oil.

Methyl 2,6 - di - 0 - mesyl - α - D - glucopyranoside **22**.

Finely powdered **13** (0.485 g, 2.5 mmol) was stannylated with $(Bu_3Sn)_2O$ (2.25 g, 3.75 mmol) in toluene (50 ml) under reflux for 5 hr. To the cooled soln was added MsCl (859 mg, 7.5 mmol) and the mixture was stirred for 70 hr at 50°. Usual work-up and

[a] These values denote $\Delta\delta_C = \delta_C$ (**15** in $CDCl_3$) − δ_C (**13** in D_2O).
[b] These values denotes $\Delta\delta_C = \delta_C$ (**19** in $CDCl_3$) − δ_C (**13** in D_2O).

chromatography over SiO_2 (100 g, toluene–EtOAc, 1:3) afforded **22** (660 mg, 75.4%) as an oil. $[\alpha]_D$ + 75.9° (c = 0.415), R_f: 0.50 in $CHCl_3$–MeOH (10:1) and 0.12 in EtOAc–toluene (3:1). (Found: C, 30.69; H, 5.06. $C_9H_{18}O_{10}S_2$ requires: C, 30.85; H, 5.18%).

Methyl 3,6-*di*-0-*benzoyl*-β-D-*galactopyranoside* **25** *and methyl* 2,3,6-*tri*-0-*benzoyl*-β-D-*galactopyranoside* **26**

Finely powdered **23** (0.485 g, 2.5 mmol) was stannylated with $(Bu_3Sn)_2O$ (2.25 g, 3.75 mmol) in toluene (30 ml) for 3.5 hr at 140°. To the cooled soln was added BzCl (1.05 g, 7.5 mmol) at 20°C and the mixture was stirred for 5 hr at 20–25°. Usual work-up and chromatography over SiO_2 (100 g, toluene–EtOAc, 3:1) gave **26** (60 mg, 4.7%). Crystals from EtOAc–i-Pr_2O, m.p. 142–145°. $[\alpha]_D$ + 50.7° (c = 0.475), R_f: 0.56 in toluene–EtOAc (3:1). NMR δ_H ($CDCl_3$–D_2O): 5.79(1 H, dd, J = 8, 10 Hz, H-2), 5.37(1 H, dd, J = 3, 10 Hz, H-3), 4.76 – 4.62(3H, m, H-6, H-6', H-1), 4.37(1H, bd, J = 3 Hz, H-4), 4.10(1H, bt, J = 7 Hz, H-5), 3.54(3H, s, OMe). (Found: C, 66.31; H, 5.20. $C_{28}H_{26}O_9$ requires: C, 66.39; H, 5.17%). Further elution with the same solvent gave **25** (954 mg, 95%). Crystals from EtOAc-i-Pr_2O, m.p. 132–133°. $[\alpha]_D$ – 7.1° (c = 0.850), R_f: 0.25 in toluene–EtOAc (3:1). NMR δ_H ($DCDl_3$–D_2O): 5.13(1H, dd, J = 3, 10 Hz, H-3), 4.70 – 4.50(2H, m, H-6, H-6'), 4.36(1H, d, J = 8 Hz, H-1), 3.57(3H, s, OMe). δ_C: 104.2 ($^1J_{CH}$ = 159.9 Hz, C-1, −0.8[c]), 75.5(C-3, +1.3), 72.4(C-5, −3.8[c]), 69.1 (C-2, −3.0[c]), 67.2(C-4, −2.8[c]), 63.0(C-6, +0.7[c]), 57.2(OMe). (Found: C, 62.59; H, 5.54. $C_{21}H_{26}O_6$ requires: C, 62.68; H, 5.51%).

Methyl 2,3,6-*tri*-0-*benzoyl*-α-D-*galactopyranoside* **30**, *methyl* 2,6-*di*-0-*benzoyl*-α-D-*galactopyranoside* **31**, *methyl* 3,6-*di*-0-*benzoyl*-α-D-*galactopyranoside* **32**, *and methyl* 6-0-*benzoyl*-α-D-*galactopyranoside* **33**

Compound **27** (0.485 g, 2.5 mmol) was stannylated with $(Bu_3Sn)_2O$ (2.25 g, 3.75 mmol) in toluene (50 ml). To the cooled soln was added BzCl (1.05 g, 7.5 mmol) at 20° and the mixture was stirred for 24 hr at 20°. The ppt was collected to give **33** (163 mg, 21.9%). Crystals from EtOA–i-Pr_2O, m.p. 152–155°. $[\alpha]_D$ + 117.8° (MeOH, c = 0.41), R_f: 0.05 in toluene–EtOAc (1:3). (Found: C, 56.41; H, 6.05. $C_{14}H_{18}O_7$ requires: C, 56.37; H, 6.08%). The filtrate was concentrated *in vacuo* and the residue was chromatographed over SiO_2 (100 g, toluene–EtOAc, 1:3) to give **30** (506 mg, 40.0%). Crystals from pentane, m.p. 137–139°. $[\alpha]_D$ + 116.9° (c = 0.415), R_f: 0.75 in toluene–EtOAc (1:1). NMR δ_H: 5.74(2H, m, H-2, H-3), 5.23 (1H, d, J = 3 Hz, H-1), 3.44(3H, s, OMe). (Found: C, 66.22; H, 5.15. $C_{28}H_{26}O_9$ requires: C, 66.39; H, 5.17%). Further elution with the same solvent afforded a crystalline mixture (302 mg, 31%) of **31** and **32** in a ratio of 1:2, judged by ^1H NMR data, R_f: 0.56 in EtOAc–toluene (3:1). NMR δ_H (**30**): 5.13(1H, q, J = 4, 10 Hz, H-2), 3.57(3H, s, OMe). δ_H (**31**): 5.33(1H, q, J = 3, 10 Hz, H-3), 4.92(1H, d, J = 4 Hz, H-1), 3.46(3H, s, OMe). (Found: C, 62.56; H, 5.55. $C_{21}H_{22}O_8$ requires: C, 62.68; H, 5.51%).

Methyl 3,6 - *di* - 0 - *benzoyl* - α - D - *mannopyranoside* **36**

Finely powdered **34** (0.485 mg, 2.5 mmol) was stannylated with $(Bu_2Sn)_2O$ (2.25 g, 3.75 mmol) in toluene (20 ml). To the cooled soln was added BzCl (1.05 g, 7.5 mmol) at 0° and the mixture was stirred for 3 hr at 20°. Usual workup and chromatography over SiO_2 (100 g, toluene–EtOAc, 3:1) gave **36** (907 mg, 90.2%). Crystals from EtOAc–i-Pr_2O, m.p. 134–136°. R_f: 0.5 in toluene–EtOAc (1:1). $[\alpha]_D$ + 58.1° (c = 0.42). NMR δ_H: 5.38(1H, dd, J = 3, 9 Hz, H-3), 4.79(1H, d, J = 2 Hz, H-1), 3.42(3H, s, OMe). δ_C: 100.7($^1J_{CH}$ = 169.7 Hz, C-1, −1.5[d]), 75.0(C-3, +2.9[d]), 70.9(C-5, −3.0[d]), 69.2(C-2, −2.2[d]), 65.8(C-4, −2.5[d]), 64.1(C-6, +1.6[d]), 54.9 (OMe). (Found: C, 62.54; H, 5.54. $C_{21}H_{22}O_8$ requires: C, 62.68; H, 5.51%). Direct crystallization of the oily product obtained after concentration of mixture, without going through chromatography, from i-Pr_2O afforded **36** in a yield of 75–80%.

Methyl 3,6 - *di* - 0 - *benzoyl* - 1 - *deoxy* - 1 - *thio* - α - D - *mannopyranoside* **39** *and methyl* 2,3,6 - *tri* - 0 - *benzoyl* - 1 - *deoxy* - 1 - *thio* - α - D - *mannopyranoside* **40**

Compound **37** (525 mg, 2.5 mmol) was stannylated with $(Bu_3Sn)_2O$ (2.25 g, 3.75 mmol) in toluene (25 ml) for 2 hr at 140°. To the cooled soln was added BzCl (1.05 g, 7.5 mmol) at 20° and the mixture was stirred for 18 hr at 25°. Usual work-up and chromatography over SiO_2 (100 g, toluene–EtOAc, 4:1) gave **40** (170 mg, 12%). $[\alpha]_D$ + 40.0° (c = 0.635), R_f: 0.70 in toluene–EtOAc (3:1). NMR δ_H: 5.73(1H, dd, J = 2, 3 Hz, H-2), 5.57(1H, dd, J = 3, 9 Hz, H-3), 5.38(1H, d, J = 2 Hz, H-1), 4.92(1H, dd, J = 3, 12 Hz, H-6), 4.62(1H, dd, J = 2, 12 Hz, H-6'), 4.56-4.24(2H, m, H-4 and H-5), 2.22(3H, s, SMe). (Found: C, 64.27; H, 5.07; S, 5.64. $C_{28}H_{26}O_8S$ requires: C, 64.36; H, 5.02; S, 6.12%). Further elution with the same solvent afforded **39** (694 mg, 66.4%). Crystals from i-Pr_2O, m.p. 132–134°. $[\alpha]_D$ + 120.6° (c = 0.452), R_f: 0.30 in toluene–EtOAc (3:1). NMR δ_H: 5.33(1H, q, J = 3, 9 Hz, H-3), 5.22(1H, d, J = 2 Hz, H-1), 2.13 (SMe). (Found: C, 60.23; H, 5.28; S, 7.49. $C_{21}H_{22}O_7S$ requires: C, 60.28; H, 5.30; S, 7.08%).

Methyl 3,6 - *di* - 0 - *benzoyl* - 1 - *deoxy* - 1 - *thio* - β - D - *galactopyranoside* **43** *and methyl* 2,3,6 - *tri* - 0 - *benzoyl* - 1 - *deoxy* - 1 - *thio* - β - D - *galactopyranoside* **44**

Compound **42** (525 mg, 2.5 mmol) was stannylated with $(Bu_3Sn)_2O$ (2.25 g, 3.75 mmol) in toluene (20 ml) for 2 hr at 140°. To a cooled soln was added BzCl (1.05 g, 7.5 mmol) at 20° and the mixture was stirred for 18 hr at 20°. Toluene was evaporated *in vacuo* and the residue was triturated with i-Pr_2O to give crystalline **43** (840 mg, 81.4%). The filtrate was evaporated and the residue was chromatographed over SiO_2 (100 g, toluene–EtOAc, 4:1) to give **44** (33 mg, 2.7%). $[\alpha]_D$ + 3.3° (c = 3.19), R_f 0.5 in toluene–EtOAc (3:1). (Found: C, 64.02; H, 5.00; S, 6.12. $C_{28}H_{26}O_8S$ requires: C, 64.36; H, 5.02; S, 6.12%). Further elution with the same solvent afforded **43** (150 mg, 14.3%). Total yield was 95.7%. Crystals from i-Pr_2O-EtOAc, m.p. 162–164°. $[\alpha]_D$ + 3.0° (c = 0.495), R_f: 0.25 in toluene–EtOAc (3:1). NMR δ_H: 5.14(1H, dd, J = 3, 10 Hz, H-3), 2.26(3H, s, SMe). (Found: C, 60.48; H, 5.28; S, 7.37. $C_{21}H_{22}O_7S$ requires: C, 60.28; H, 5.30; S, 7.65%).

2,3,6,1',6'-*Penta*-0-*benzoyl*-*sucrose* 46

Finely powdered **45** (0.85 g, 2.5 mmol) was stannylated with $(Bu_3Sn)_2O$ (4.5 g, 7.5 mmol) in toluene (50 ml) for 4 hr at 140°. To the cooled soln was added BzCl (2.1 g, 15 mmol) at 20° and the mixture was stirred for 5 days at 20–25°, evaporated *in vacuo*, and subjected to chromatography over SiO_2 (100 g, toluene–EtOAc, 1:1, twice) to give **46** (1.87 g, 87%). $[\alpha]_D$ + 63.2° (c = 0.525), R_f: 0.56 in toluene–EtOAc (1:3) and 0.50 in $CHCl_3$–MeOH (10:1). NMR δ_H: 6.01(1H, t, J = 10 Hz, H-3), 5.94(1H, d, J = 4 Hz, H-1), 5.33(1H, dd, J = 4, 10 Hz, H-2). δ_C (50°): 103.2 (C-2'), 90.0($^1J_{CH}$ = 173, 3 Hz, C-1), 79.4(C-4'), 78.7(C-3'), 65.3(C-1'), 64.2(C-6'), 63.8(C-6). (Found: C, 65.52; H, 5.00. $C_{47}H_{42}O_{16}$ requires: C, 65.42; H, 4.91%).

2,3,6,2',3',6' - *Hexa* - 0 - *benzoyl* - α,α' - *trehalose* **48**

Finely powdered α,α'-trehalose (1.89 g, 5 mmol) was stannylated with $(Bu_3Sn)_2O$ (9.0 g, 15 mmol) in toluene (50 ml) for 24 hr at 140°. To a cooled soln was added BzCl (4.2 g, 30 mmol) at 20° and the mixture was stirred for 20 hr at 50°. Usual work-up and chromatography over SiO_2 (100 g, toluene–EtOAc, 2:1, twice) afforded hexabenzoate (3.536 g, 73.1%). $[\alpha]_D$ + 173.6°(c = 0.435), R_f: 0.62 in toluene-EtOAc (1:1). NMR δ_H: 5.91(2H, t, J = 10 Hz, H-3, H-3'), 5.58(2H, d, J = 4 Hz, H-1, H-1'), 5.43(2H, dd, J = 4, 10 Hz, H-2, H-2'). δ_C: 93.2($^1J_{CH}$ = 175.8 Hz, C-1, C-1'), 73.4, 71.0, 70.6, 69.1 and 62.5 (C-6, C-6'). (Found: C, 66.43; H, 4.88. $C_{54}H_{46}O_{17}$ requires: C, 67.07; H, 4.80%).

2,6,3',6'-*Tetra*-0-*benzoyl*-*lactose* **51**

Finely powdered lactose (1.08 g, 3 mmol) was stannylated with $(Bu_3Sn)_2O$ (5.8 g, 9.5 mmol) in toluene (50 ml) for 3 hr at 140°. To a cooled soln was added BzCl (2.8 g, 19.8 mmol) and the mixture was stirred for 2 days at 45°. Upon cooling, a white ppt was collected, washed with toluene to give **51** (1.0 g). The filtrate was diluted with n-hexane to give a further ppt (2.0 g). A major component of this ppt was isolated by chromatography over SiO_2 (100 g, toluene–EtOAc, 2:1) to give **51** (722 mg, combined yield

[c] These values denotes $\Delta\delta_c$ (**25** in $CDCl_3$) – δ_C (**23** in D_2O).
[d] These values denote $\Delta\delta = \delta_C$ (**36** in $CDCl_3$) – δ_C (**34** in D_2O).

was 71.9%) m.p. 221–224°. $[\alpha]_D$ +73.3° (c = 0.45), $[\alpha]_D$ did not change after standing for 7 days at 20°, R_f: 0.37 in toluene–EtOAc (1:1). NMR δ_C (DMSD-d_6, 60°): 89.2($^1J_{CH}$ = 169.7 Hz, C-1, −1.7[e]), 72.8(C-2, +1.5[e]), 68.8(C-3, −6.1[e]), 80.3(C-4, −0.7[e]), 67.7(C-5, −7.0[e]), 63.6(C-6, +3.2[e]), 103.4($^1J_{CH}$ = 161.1 Hz, C-1′, −0.1[e]), 67.4(C-2′, −3.4[e]), 76.2(C-3′, +2.9[e]), 66.0(C-4′, −2.2[e]), 74.0(C-5′, −1.4[e]), 63.9(C-6′, +3.0[e]). (Found: C, 63.23; H, 5.01. $C_{40}H_{38}O_{15}$ requires: C, 63.32; H, 5.05%).

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