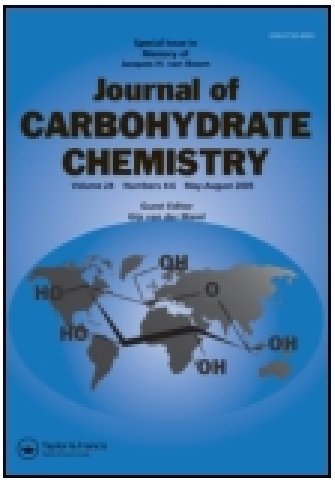

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Efficient Palladium(0)-Catalyzed Synthesis of Alkenyl 1-Thioglycosides and Thiodisaccharides

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EFFICIENT PALLADIUM(0)-CATALYZED SYNTHESIS OF ALKENYL 1-THIOGLYCOSIDES AND THIODISACCHARIDES

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ABSTRACT

Unsaturated thiodisaccharides are obtained in good yields by alkylation of ethyl α-*O*-Δ^2-glycosides, having a leaving group at C-4, with various thiocarbohydrates in the presence of a catalytic amount of palladium(0). The reaction is regio- and stereospecific for the α-*erythro* enoside, and only stereospecific in the case of the α-*threo* enoside, alkylation occurring at C-4 and C-2. In all cases, only the β-anomer is formed.

INTRODUCTION

Current interest in thioglycosides rests in their use in glycoside synthesis,[1] in their biological properties and particularly their increased stability towards enzymatic degradation, as well as their potential values in affinity chromatography. There are several methods to synthesize such compounds from acylated glycosyl halides, acetylated

glycosides or methyl glycosides.[2] We have recently shown that alkenyl glycosides could be obtained very efficiently and under very mild conditions in the presence of a palladium-catalyst.[3] This methodology was extended to the preparation of di- and trisaccharides.[4]

Palladium-catalyzed formation of carbon-sulfur bonds is less common than formation of carbon-oxygen bonds.[5] However, we[6] and Moreno-Manas and co-workers[7] have shown that thiols react cleanly and quantitatively with allylic carbonates in the presence of a catalytic amount of palladium(0) to give the corresponding allylic alkyl sulfides, a breakthrough in the palladium-catalyzed formation of a carbon-sulfur bond. We expected that this new methodology could be used in carbohydrate chemistry in order to prepare alkenyl thiosaccharides and thiodisaccharides, and in this paper we report our recent work in this field.

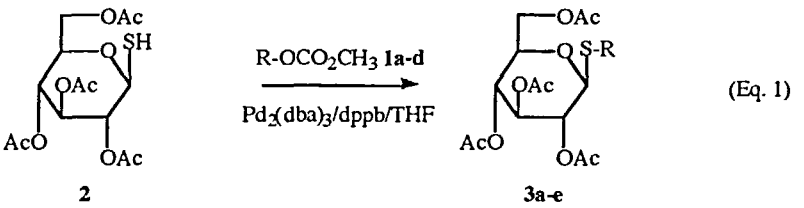
RESULTS AND DISCUSSION

Reaction of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-glucopyranose (**2**) with cinnamyl methyl carbonate (**1a**) or methallyl methyl carbonate (**1b**) in the presence of $Pd_2(dba)_3$ [tris(dibenzylidenacetone)dipalladium] and dppb [1,4-bis(diphenylphosphino)butane] in THF at 60 °C gave the corresponding alkenyl 1-thio-D-glucopyranosides **3a** and **3b** having the β-configuration in 100% and 68% yield, respectively (Eq. 1). The β anomeric configuration was readily derived from the ^{1}H NMR data; we observed for H-1 a doublet with a coupling constant $J_{1,2}$ = 9.6 and 10.2 Hz, respectively, characteristic for a β configuration.[8]

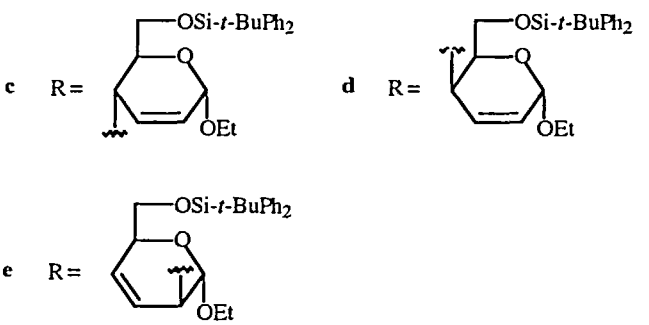
The reaction of 1-thiosugar **2** with α-D-*erythro* enoside **1c** gave regio- and stereospecifically the thiodisaccharide **3c**, arising from the coupling at C-4, albeit in low yield (18%), even after 70 h. The β configuration of the glucopyranose moiety was derived from the ^{1}H NMR data; we observed for H-1' a doublet at δ 4.73 with a coupling constant $J_{1',2'}$ = 10.2 Hz. The alkylation at C-4 was confirmed by the upfield shift of H-4 in compound **3c** by comparison with its oxygen analog (δ = 3.70 ppm and 4.28 ppm,[4b] respectively), and from the upfield shift of C-4 at 39.5 ppm. The overall retention of configuration at C-4, as expected from our precedent stereochemical studies,[6a] was also observed from the ^{1}H NMR data; the coupling constant $J_{4,5}$ = 10.2 Hz is characteristic for a *trans* diaxial relationship between H-4 and H-5.

When the α-D-*threo* enoside **1d** was used as the π-allyl precursor, a mixture of the 4-*S*-alkylated-2,3-unsaturated carbohydrate **3d** and its 2-*S*-alkylated-3,4-unsaturated isomer **3e** was obtained with 49% yield in both cases. The structures of these two

compounds were assigned through their ^{1}H and ^{13}C NMR data and their comparison with the data from ethyl 2,3,4-trideoxy-6-*O*-(*tert*-butyldimethylsilyl)-4-*S*-(2-benzothiazolyl)-4-thio-α-D-*threo*-hex-2-enopyranoside and methyl 2,3,4-trideoxy-6-*O*-(*tert*-butyldimethylsilyl)-2-*S*-(2-benzothiazolyl)-2-thio-α-D-*threo*-hex-3-enopyranoside.[9] The main characteristic differences between **3d** and **3e** are the chemical shifts of H-4 and C-4 at δ 3.35 ppm and 43.6 ppm, respectively, for **3d**, and H-2 and C-2 at δ 3.36 ppm and 42.4 ppm, respectively, for compound **3e**. The observed downfield shift for C-1 in compound **3e** (δ = 101.8 ppm) is also characteristic for 3,4-unsaturation.[10] Finally, in compound **3d**, the magnitude of $J_{4,5}$ = 3.1 Hz indicated a quasi-equatorial-axial geometry for H-4 and H-5 and is consistent with the *threo* configuration, while the coupling constant $J_{1,2}$ < 1 Hz for **3e** is consistent with an equatorial-quasi-equatorial arrangement of H-1 and H-2.



a R = *(E)*-C_6H_5-CH=CH-CH_2- **b** R = CH_2=C(CH_3)CH_2-



Scheme 1

In order to check that this new methodology was not limited to 1-thio carbohydrates, we used methyl 2,3,6-tri-*O*-benzoyl-4-thio-α-D-galactopyranoside (**4**) as the nucleophile in this alkylation reaction (Eq. 2). Condensation of **4** with cinnamyl methyl carbonate **1a** gave as expected the 4-*S*-cinnamyl-4-thio-galactopyranoside **5a** in 82% yield, although reaction with α-D-*erythro* enoside **1c** gave regio- and stereospecifically the thio-disaccharide **5c** in 70% yield. The assignment of the structure was again based on ^{1}H and ^{13}C NMR data; the ^{13}C NMR spectra of the unsaturated moiety of **5c** is very similar to that of **3c**, and particularly the chemical shifts of C-1 and C-4 at δ 93.5 ppm and 38.8 ppm, respectively. The coupling constants $J_{1',2'} = 4.2$ Hz and $J_{4,5} = 10.2$ Hz are characteristic of a β-configuration and an α-D-*threo*-hex-2-enopyranose structure, respectively.

Coupling of the α-D-*threo* enoside **1d** and the thiol **4** gave a mixture of the 4-*S*-alkylated-2,3-unsaturated carbohydrate **5d** and its 2-*S*-alkylated-3,4-unsaturated isomer **5e** in 17% and 39% yield, respectively. The structures of these two compounds were again assigned through their ^{1}H and ^{13}C NMR data. Compounds **5d** and **5e** exhibited chemical shifts for H-4 and C-4 at δ 3.30-3.46 ppm and 39.3 ppm, respectively, for **5d**, and H-2 and C-2 at δ 3.61 ppm and 42.9 ppm, respectively, for compound **5e**.

This difference in regioselectivity in the palladium-catalyzed alkylation reaction between the α-D-*erythro* and the α-D-*threo* enopyranoside can be rationalized as previously suggested.[4b] The first step is the formation of the π-allyl complex by oxidative addition to palladium(0), which occurs with inversion of configuration. In the case of the π-allyl palladium species obtained from the *erythro* compound, the attack of the thiolate occurs only at C-4, the C-2 position being too crowded. Conversely, the position at C-2 of the π-allyl intermediate obtained from the *threo* compound is less crowded and *S*-alkylation can occur at this position together with *S*-alkylation at C-4.

CONCLUSION

In conclusion, we have extended our previously published palladium-catalyzed access to disaccharides to the synthesis of thiodisaccharides. 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranose or methyl 2,3,6-tri-*O*-benzoyl-4-thio-α-D-galactopyranoside reacted with ethyl 6-*O*-*tert*-butyldiphenylsilyl-4-*O*-methoxycarbonyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside in the presence of a catalytic amount of palladium(0) to give regio- and stereospecifically the β-thiodisaccharide, the alkylation occurring at C-4 of the unsaturated carbohydrate. In the case of ethyl 6-*O*-*tert*-butyldiphenylsilyl-4-*O*-methoxy-carbonyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside, the reaction is stereospecific but

not regiospecific, alkylation occuring at C-2 and C-4 to give the thiodisaccharides having the β-configuration .

EXPERIMENTAL

General methods. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates (60 F-254, Merck). Compounds were visualized under UV light (254 nm) or by spraying with an H_2SO_4 solution and heating. Column chromatography was performed on silica gel 60 (40-63 mesh, Merck). NMR spectra were recorded on Bruker AC 200, AM 300 and AM 500 spectrometers, and chemical shifts are given in ppm on the δ scale from internal tetramethylsilane (H' refers to the saturated moiety of the thiodisaccharide). Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Reactions involving palladium complexes were carried out in a Schlenk tube under a nitrogen atmosphere. THF was distilled from sodium/benzophenone and stored under a nitrogen atmosphere. $Pd_2(dba)_3$, 1,4-bis(diphenylphosphino)butane and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**2**) are from a commercial source. Methyl 2,3,6-tri-*O*-benzoyl-4-thio-α-D-galactopyranoside (**4**),[11] ethyl 6-*O*-tert-butyldiphenylsilyl-4-*O*-methoxycarbonyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1c**),[4b] and ethyl 6-*O*-tert-butyldiphenylsilyl-4-*O*-methoxycarbonyl-2,3-dideoxy-α-D-*threo*-hex-2-enopyranoside (**1d**)[4b] were prepared according to literature procedures.

General Procedure for Palladium-Catalyzed *S*-Alkylation Procedure. The catalytic system was prepared by stirring $Pd_2(dba)_3$ (22.9 mg, 0.025 mmol) and dppb (42.6 mg, 0.1 mmol) in tetrahydrofuran (5 mL) for 1 h in a Schlenk tube under argon. This solution was added under argon to a Schlenk tube containing the unsaturated carbonate (2 mmol) and the thiocarbohydrate (1 mmol) in tetrahydrofuran (5 mL). The solution was stirred at 60 °C and the reaction followed by TLC. After 24 h, the solvent was evaporated under reduced pressure to give an oil that was purified by column chromatography on silica gel to give the thioether.

***(E)*-Cinnamyl Tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (3a)**: yield 100%; mp 112-115 °C; R_f 0.28 (hexane/ethyl acetate 7/3); $[\alpha]^{20}_D$ -74 (*c* 2.5, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 2.00 (s, 3H, $COCH_3$), 2.01 (s, 3H, $COCH_3$), 2.06 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$), 3.40 (dd, 1H, J = 13.5 and 6.3 Hz, SCH_2), 3.54-3.70 (m, 2H, SCH_2, H-5), 4.12 (dd, 1H, J = 12.2 and 2.2 Hz, H-6), 4.24 (dd, 1H, J = 12.2 and 5.0 Hz, H-6), 4.51 (d, 1H, J = 9.6 Hz, H-1), 5.02-5.26 (m, 3H, H-2, H-3, H-4), 6.10-6.26 (m, 1H, -CH=), 6.49 (d, 1H, J = 15.7 Hz, -CH=), 7.27-7.39 (m, 5H, C_6H_5);

^{13}C (75 MHz, $CDCl_3$) δ 20.7 (2xCH_3), 20.8 (CH_3), 20.8 (CH_3), 32.6 (SCH_2), 62.6 (C-6), 68.8 (C-4), 70.3 (C-2), 74.3 (C-5), 76.2 (C-3), 82.4 (C-1), 125.3, 127.1, 128.6, 129.4 and 133.9 (-CH=, C_6H_5), 137.2 (-CH=), 170.4 (2xCO), 171.3 (CO), 171.6 (CO).

Anal. Calcd for $C_{23}H_{28}O_9S$ (480.53): C, 57.49; H, 5.87; S, 6.67. Found: C, 57.39; H, 5.82; S, 6.29.

Methallyl Tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (3b): yield 68%; mp 50-52 °C; $[\alpha]^{20}_D$ -12 (*c* 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 1.81 (s, 3H, =C-CH_3), 2.01 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 2.05 (s, 3H, $COCH_3$), 2.09 (s, 3H, CH_3), 3.12 (d, 1H, *J* = 13.2 Hz, SCH_2), 3.45 (d, 1H, *J* = 13.2 Hz, SCH_2), 3.59-3.68 (m, 1H, H-5), 4.12 (dd, 1H, *J* = 12.2 and 2.0 Hz, H-6), 4.23 (dd, 1H, *J* = 12.2 and 5.1 Hz, H-6), 4.46 (d, 1H, *J* = 10.2 Hz, H-1), 4.86 (s, 1H, =CH_2), 4.89 (s, 1H, =CH_2), 5.01-5.28 (m, 3H, H-2, H-3, H-4); ^{13}C (75 MHz, $CDCl_3$) δ 20.4 (2xCH_3), 20.6 (2xCH_3), 37.6 (SCH_2), 62.2 (C-6), 68.4 (C-4), 69.8 (C-2), 73.9 (C-5), 75.7 (C-3), 81.8 (C-1), 114.6 (=CH_2), 140.4 (>C=), 169.4 (2xCO), 170.2 (CO), 170.6 (CO).

Methyl 4-Deoxy-4-*S*-(*E*)-cinnamyl-4-thio-2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside (5a): yield 82%; oil; R_f 0.47 (hexane/ethyl acetate 7/3); $[\alpha]^{20}_D$ -36 (*c* 0.5, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 3.26 (d, 2H, *J* = 7.1 Hz, SCH_2), 3.40 (s, 3H, $COCH_3$), 3.65 (dd, 1H, *J* = 4.6 Hz, H-4), 4.52 (dd, 1H, *J* = 10.3 and 4.2 Hz, H-6), 4.61 (m, 1H, H-5), 4.74 (dd, 1H, *J* = 10.3 and 6.4 Hz, H-6), 5.18 (d, 1H, *J* = 3.9 Hz, H-1), 5.68 (dd, 1H, *J* = 10.7 and 3.9 Hz, H-2), 5.88 (dd, 1H, *J* = 10.7 and 4.6 Hz, H-3), 6.00 (dt, 1H, *J* = 16.9 and 7.1 Hz, -CH=), 6.15 (d, 1H, *J* = 16.9 Hz, -CH=), 7.00-8.10 (m, 20H, C_6H_5); ^{13}C (75 MHz, $CDCl_3$) δ 35.5 (SCH_2), 47.3 (C-4), 55.3 (CH_3), 65.1 (C-6), 67.8 (C-5), 70.3 and 70.9 (C-2, C-3), 97.5 (C-1), 124.7, 126.3, 127.6, 128.4, 128.5, 128.6, 129.3, 129.4, 129.6, 129.7, 129.8, 133.1, 133.2, 133.4 and 133.5 (-CH=, C_6H_5), 136.1 (-CH=), 165.8 (CO), 165.9 (CO), 166.1 (CO).

Anal. Calcd for $C_{37}H_{34}O_8S$ (638.74): C, 69.57; H, 5.37; S, 5.02. Found: C, 69.40; H, 5.27; S, 4.83.

Ethyl 6-*O*-*tert*-Butyldiphenylsilyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-1-β-D-glucopyranosyl)-4-thio-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (3c): yield 18%; oil; R_f 0.5 (hexane/ethyl acetate 1/1); $[\alpha]^{20}_D$ +36 (*c* 0.1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9H, CMe_3), 1.22 (t, 3H, *J* = 7.1 Hz, CH_2CH_3), 1.96 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 2.20 (s, 3H, $COCH_3$), 3.56 (dq, 1H, *J* = 9.6 and 7.1 Hz, CH_2CH_3), 3.62 (ddd, 1H, *J* = 9.9, 4.6 and 2.0 Hz, H-5'), 3.70 (bd, 1H, *J* = 10.2 Hz, H-4), 3.84 (dq, 1H, *J* = 9.6 and 7.1 Hz, CH_2CH_3), 4.00 (m, 2H, H-6, H-6'), 4.07 (m, 2H, H-5, H-6), 4.24 (dd, 1H, *J* = 12.5 and 4.6 Hz, H-6'), 4.73 (d, 1H, *J* = 10.2 Hz, H-1'), 4.99 (dd, 1H, *J* = 10.2 and 9.3 Hz, H-2'), 5.07

(bs, 1H, H-1), 5.09 (dd, 1H, J = 9.9 and 9.3 Hz, H-4'), 5.21 (dd, 1H, J = 9.3 and 9.3 Hz, H-3'), 5.94 (m, 2H, H-2, H-3), 7.39-7.46 (m, 6H, C_6H_5), 7.74-7.77 (m, 4H, C_6H_5); ^{13}C (75 MHz, $CDCl_3$) δ 15.3 (CH_2CH_3), 19.4 (CMe_3), 20.6 (2xCH_3), 20.7 (2xCH_3), 26.8 (CMe_3), 39.5 (C-4), 61.8 (C-6'), 63.5 (C-6), 63.6 (CH_2CH_3), 68.0 (C-4'), 70.1 (C-2'), 71.7 (C-5), 74.0 (C-3'), 75.5 (C-5'), 82.6 (C-1'), 93.7 (C-1), 128.7 (C-2), 131.3 (C-3), 127.7, 127.8, 129.7, 133.2, 133.7, 135.6 and 135.9 (C_6H_5), 169.3 (CO), 169.4 (CO), 170.2 (CO), 170.6 (CO).

Anal. Calcd for $C_{38}H_{50}O_{12}SSi$ (758.96): C, 60.14; H, 6.64; S, 4.22. Found: C, 60.09; H, 6.62; S, 3.77.

Ethyl 6-*O*-*tert*-Butyldiphenylsilyl-4-*S*-(2,3,4,6-tetra-*O*-acetyl-1-β-D-glucopyranosyl)-4-thio-2,3,4-trideoxy-α-D-*threo*-hex-2-enopyranoside (3d): yield 49%; oil; R_f 0.19 (hexane/ethyl acetate 7/3); $[\alpha]^{20}_D$ -99 (c 1, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H, CMe_3), 1.25 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.69 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 2.03 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$), 3.35 (ddd, 1H, J = 5.1, 3.1 and 1.2 Hz, H-4), 3.49 (ddd, 1H, J = 9.7, 5.5 and 2.4 Hz, H-5'), 3.55 (dq, 1H, J = 9.7 and 7.3 Hz, CH_2CH_3), 3.90 (m, 2H, H-6), 4.04 (dd, 1H, J = 12.2 and 2.4 Hz, H-6'), 3.92 (dq, 1H, J = 9.7 and 7.3 Hz, CH_2CH_3), 4.15 (dd, 1H, J = 12.2 and 5.5 Hz, H-6'), 4.46 (ddd, 1H, J = 6.1, 3.1 and 3.1 Hz, H-5), 4.83 (d, 1H, J = 10.4 Hz, H-1'), 4.93 (dd, 1H, J = 10.4 and 9.1 Hz, H-2'), 5.02 (dd, 1H, J = 9.7 and 9.7 Hz, H-4'), 5.07 (d, 1H, J = 3.0 Hz, H-1), 5.17 (dd, 1H, J = 9.7 and 9.1 Hz, H-3'), 5.88 (ddd, 1H, J = 9.8, 3.0 and 1.2 Hz, H-2), 6.24 (dd, 1H, J = 9.8 and 5.1 Hz, H-3), 7.40-7.47 (m, 6H, C_6H_5), 7.68-7.72 (m, 4H, C_6H_5); ^{13}C (50 MHz, CD_3OD) δ 15.6 (CH_2CH_3), 19.8 (CMe_3), 20.4 (CH_3), 20.5 (2xCH_3), 20.7 (CH_3), 27.2 (CMe_3), 40.9 (C-4), 63.1 (C-6'), 64.2 (CH_2CH_3), 66.3 (C-6), 69.6 (C-4'), 71.4 (C-2'), 72.0 (C-5), 75.2 (C-3'), 76.6 (C-5'), 83.7 (C-1'), 95.4 (C-1), 127.1 (C-2), 131.3 (C-3), 128.8, 128.9, 130.9, 134.3, 134.4, 136.5 and 136.6 (C_6H_5), 170.7 (CO), 171.0 (CO), 171.3 (CO), 171.9 (CO).

Anal. Calcd for $C_{38}H_{50}O_{12}SSi$ (758.96): C, 60.14; H, 6.64; S, 4.22. Found: C, 60.18; H, 6.59; S, 3.83.

Ethyl 6-*O*-*tert*-Butyldiphenylsilyl-2-*S*-(2,3,4,6-tetra-*O*-acetyl-1-β-D-glucopyranosyl)-2-thio-2,3,4-trideoxy-α-D-*threo*-hex-3-enopyranoside (3e): yield 49%; oil; R_f 0.34 (hexane/ethyl acetate 7/3); $[\alpha]^{20}_D$ +6 (c 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.09 (s, 9H, CMe_3), 1.25 (t, 3H, J = 7.3 Hz, CH_2CH_3), 2.03 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 2.06 (s, 6H, 2 x $COCH_3$), 3.36 (ddd, 1H, J = 4.3, 1.8 and 1.8 Hz, H-2), 3.55 (dq, 1H, J = 9.7 and 7.3 Hz, CH_2CH_3), 3.59 (ddd, 1H, J = 10.4, 4.9 and 1.8 Hz, H-5'), 3.65 (dd, 1H, J = 10.0 and 7.0 Hz, H-6), 3.75 (dq, 1H, J = 9.7 and 7.3 Hz, CH_2CH_3), 3.81 (dd, 1H, J = 10.0 and 5.8 Hz, H-6), 4.08 (dd,

1H, J = 12.2 and 1.8 Hz, H-6'), 4.23 (dd, 1H, J = 12.2 and 4.9 Hz, H-6'), 4.23 (m, 1H, H-5), 4.55 (d, 1H, J = 10.1 Hz, H-1'), 5.06 (dd, 1H, J = 10.1 and 9.2 Hz, H-2'), 5.08 (dd, 1H, J = 9.8 and 9.8 Hz, H-4'), 5.13 (bs, 1H, H-1), 5.21 (dd, 1H, J = 9.8 and 9.2 Hz, H-3'), 5.72 (ddd, 1H, J = 10.4, 4.3 and 1.8 Hz, H-3), 6.05 (bd, 1H, J = 10.4 Hz, H-4), 7.40-7.49 (m, 6H, C_6H_5), 7.69-7.70 (m, 4H, C_6H_5); ^{13}C (50 MHz, CD_3OD) δ 15.6 (CH_2CH_3), 20.0 (CMe_3), 20.6 (2xCH_3), 20.8 (2xCH_3), 27.4 (CMe_3), 42.4 (C-2), 63.1 (C-6'), 64.5 (CH_2CH_3), 67.2 (C-6), 69.2 and 69.6 (C-4', C-5), 70.7 (C-2'), 75.1 (C-3'), 76.9 (C-5'), 83.0 (C-1'), 101.8 (C-1), 124.3 (C-3), 134.3 (C-4), 128.8, 129.9, 130.9 and 136.7 (C_6H_5), 170.9 (CO), 171.0 (CO), 171.4 (CO), 172.0 (CO).

Anal. Calcd for $C_{38}H_{50}O_{12}SSi$ (758.96): C, 60.14; H, 6.64; S, 4.22. Found: C, 60.24; H, 6.62; S, 3.54.

Ethyl 6-*O*-*tert*-Butyldiphenylsilyl-4-*S*-(methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranos-4-yl)-4-thio-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (5c): yield 70%; yellow solid; mp 76-78 °C; R_f 0.42 (hexane/ethyl acetate 4/1); $[\alpha]^{20}_D$ +67 (c 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.00 (s, 9H, CMe_3), 1.12 (t, 3H, J = 7.0 Hz, CH_2CH_3), 3.38 (s, 3H, OCH_3), 3.30-3.40 (m, 1H, CH_2CH_3), 3.45-3.65 (m, 4H, CH_2CH_3, H-5, H-6, H-4'), 3.69 (bd, 1H, J = 9.2 Hz, H-4), 4.07 (dd, 1H, J = 11.4 and 2.9 Hz, H-6), 4.28 (dd, 1H, J = 11.4 and 3.7 Hz, H-6'), 4.50 (m, 1H, H-5'), 4.70 (dd, 1H, J = 11.4 and 7.7 Hz, H-6'), 4.84 (bs, 1H, H-1), 5.18 (d, 1H, J = 3.7 Hz, H-1'), 5.55 (dd, 1H, J = 10.7 and 3.7 Hz, H-2'), 5.67 (ddd, 1H, J = 10.0, 2.7 and 2.7 Hz, H-2), 5.93 (dd, 1H, J = 10.7 and 4.0 Hz, H-3'), 6.00 (bd, 1H, J = 10.0 Hz, H-3), 7.13-8.08 (m, 25H, C_6H_5); ^{13}C (75 MHz, $CDCl_3$) δ 15.2 (CH_2CH_3), 19.3 (CMe_3), 26.9 (CMe_3), 38.8 (C-4), 48.6 (C-4'), 55.3 (OCH_3), 63.5 (C-6, CH_2CH_3), 65.3 (C-6'), 58.1 (C-5'), 70.4 and 70.5 (C-2', C-3'), 71.5 (C-5), 93.5 (C-1), 97.4 (C-1'), 127.5 and 131.8 (C-2, C-3), 127.8, 128.3, 128.4, 128.5, 129.1, 129.4, 129.6, 129.7, 129.8, 133.2, 133.3, 133.6, 135.8 and 135.9 (C_6H_5), 165.8 (CO), 166.0 (CO), 166.1 (CO).

Anal. Calcd for $C_{52}H_{56}O_{11}SSi$ (917.16): C, 68.10; H, 6.15; S, 3.50. Found: C, 67.60; H, 6.12; S, 3.50.

Ethyl 6-*O*-*tert*-Butyldiphenylsilyl-4-*S*-(methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranos-4-yl)-4-thio-2,3,4-trideoxy-α-D-*threo*-hex-2-enopyranoside (5d): yield 17%; oil; R_f 0.44 (hexane/ethyl acetate 4/1); $[\alpha]^{20}_D$ -44 (c 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 9H, CMe_3), 1.10 (t, 3H, J = 6.6 Hz, CH_2CH_3), 3.30-3.46 (m, 2H, H-4, CH_2CH_3), 3.36 (s, 3H, OCH_3), 3.65-3.76 (m, 2H, H-4', CH_2CH_3), 3.91 (dd, 1H, J = 10.3 and 5.9 Hz, H-6), 4.02 (dd, 1H, J = 10.3 and 6.6 Hz, H-6), 4.19 (ddd, 1H, J = 6.6, 5.9 and 2.2 Hz, H-5), 4.51-4.68 (m, 3H, H-5', H-6'), 4.90 (d, 1H, J = 2.2 Hz, H-1), 5.17 (d, 1H, J = 3.7 Hz, H-1'), 5.54 (bd, 1H, J = 10.3 Hz, H-2), 5.58 (dd, 1H, J = 11.0 and 3.7 Hz, H-2'), 5.17 (bd, 1H, J = 10.3 Hz, H-3),

5.81 (dd, 1H, J = 11.0 and 4.4 Hz, H-3'), 7.30-8.10 (m, 25H, C_6H_5); ^{13}C (75 MHz, $CDCl_3$) δ 15.2 (CH_2CH_3), 19.2 (CMe_3), 26.8 (CMe_3), 39.3 (C-4), 46.3 (C-4'), 55.3 (OCH_3), 63.3 (CH_2CH_3), 64.2 (C-6), 65.5 (C-6'), 69.2 (C-5'), 70.0 (C-2'), 70.4 (C-3'), 70.7 (C-5), 94.2 (C-1), 97.4 (C-1'), 127.5 and 129.1 (C-2, C-3), 127.7, 127.8, 128.4, 128.7, 129.5, 129.7, 129.8, 130.1, 133.1, 133.2, 133.5, 135.6 and 135.7 (C_6H_5), 166.0 (CO), 166.1 (CO).

Anal. Calcd for $C_{52}H_{56}O_{11}SSi$ (917.16): C, 68.10; H, 6.15; S, 3.50. Found: C, 68.12; H, 6.20; S, 3.21.

Ethyl 6-*O*-*tert*-Butyldiphenylsilyl-2-*S*-(methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranos-4-yl)-2-thio-2,3,4-trideoxy-α-D-*threo*-hex-3-enopyranoside (5e): yield 39%; white solid; mp 71-73 °C; R_f 0.53 (hexane/ethyl acetate 4/1); $[\alpha]^{20}_D$ +62 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3H, J = 6.6 Hz, CH_2CH_3), 1.07 (s, 9H, CMe_3), 2.73 (dq, 1H, J = 9.6 and 6.6 Hz, CH_2CH_3), 3.08 (bs, 1H, H-2), 3.42 (s, 3H, OCH_3), 3.57 (dd, 1H, J = 10.3 and 7.3 Hz, H-6), 3.61 (m, 1H, H-4'), 3.75 (dd, 1H, J = 10.3 and 5.9 Hz, H-6), 3.90 (m, 1H, H-5), 4.43 (dd, 1H, J = 11.0 and 3.7 Hz, H-6'), 4.53 (m, 1H, H-5'), 4.67 (dd, 1H, J = 11.0 and 7.3 Hz, H-6'), 4.78 (s, 1H, H-1), 5.15 (d, 1H, J = 3.7 Hz, H-1'), 5.58 (dd, 1H, J = 10.3 and 3.7 Hz, H-2'), 5.66 (dm, 1H, J = 10.4 Hz, H-3), 5.91 (bd, 1H, J = 10.4 Hz, H-4), 5.96 (dd, 1H, J = 10.3 and 3.7 Hz, H-3'), 7.30-8.10 (m, 25H, C_6H_5); ^{13}C (75 MHz, $CDCl_3$) δ 15.0 (CH_2CH_3), 19.3 (CMe_3), 27.0 (CMe_3), 42.9 (C-2), 46.8 (C-4'), 55.3 (OCH_3), 62.8 (CH_2CH_3), 65.5 (C-6'), 65.9 (C-6), 68.0 and 68.1 (C-5, C-5'), 69.3 (C-3'), 70.5 (C-2'), 97.5 (C-1'), 100.8 (C-1), 123.1, 127.8, 128.3, 128.4, 128.5, 129.5, 129.6, 129.7, 129.8, 129.9, 130.3, 132.8, 133.2, 133.5, 135.7 and 135.8 (C-3, C-4, C_6H_5), 165.7 (CO), 166.1 (CO), 166.2 (CO).

Anal. Calcd for $C_{52}H_{56}O_{11}SSi$ (917.16): C, 68.10; H, 6.15; S, 3.50. Found: C, 68.16; H, 6.03; S, 3.35.

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