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Facile synthesis of 1-thio-β-lactoside clusters scaffolded onto *p*-methoxyphenyl, β-D-galactopyranoside, β-D-glucopyranoside, and lactoside

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Abstract

The free-radical addition of 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-1-thio-β-D-glucopyranose to the allyl ether functions of *p*-methoxyphenyl per-*O*-allyl-D-galactopyranoside, D-glucopyranoside, and lactoside provides a concise and effective route for synthesis of glycoside clusters, of use for exploring anti-metastatic activity.

Keywords: Free-radical addition; 1-Thio-β-lactoside; Glycocluster; Anti-metastasis

1. Introduction

Tumor cell adhesion mediated by cell-surface carbohydrates has been suggested to play a key step in tumor cell metastasis. Carbohydrates are potential candidates[1–5] for prevention of metastatic spread by disrupting the requisite carbohydrate-initiated interactions between tumor cells and other cells, such as endothelial cells and platelets.[6] To date, application of such approaches have been frustrated by the inherent low affinity of carbohydrate ligands for their protein receptors. Because cell-surface carbohydrates typically occur as clusters, a variety of multivalent carbohydrates have been designed and prepared[7] to exploit the so-called "glycoside-cluster effect",[8,9] which apparently constitutes the best strategy for overcoming the "weak binding" problem.

Methyl β-lactoside can significantly reduce the formation of lung tumor colonies in mice.[5] To increase its efficacy, multivalent β-lactosides have been synthesized in Roy's group.[10–13] We have, therefore, prepared three lactoside clusters (**I**, **II**, and **III**), by classical radical reactions of thiols with allylic ethers, to explore their anti-metastatic activity.

2. Results and discussion

Synthesis of 1-thiolactose (**3**).—To prepare **3**, hepta-*O*-acetyl-α-lactosyl bromide (**1**) was refluxed with thiourea in acetone for 30 min (Scheme 1) but the intermediate, the 2-thiopseudourea hydrobromide (**2**) was much more difficult to crystallize than described.[14] Instead, the solution was concentrated, and then chloroform and a solution of sodium pyrosulfite in water heated at 85 °C were added to the residue. The mixture was boiled for 15 min to give the desired compound **3** in 57.8% yield in two steps and characterized by FTIR (2565 cm^{-1}, SH; 1747 cm^{-1}, CO).[15]

Synthesis of p-*methoxyphenyl per*-O-*allyl glycosides* (**6**, **9**, and **12**) *(Scheme 2).*—Compounds **4**,[16] **7**, and **10** were *O*-deacetylated to afford **5**, **8**, and **11** quantitatively. Compounds **5**, **8**, and **11** were treated with sodium hydride in anhydrous *N*,*N*-dimethylformamide (DMF) at room temperature for 15 min and then allyl bromide was added dropwise to give the corresponding compounds **6**, **9**, and **12**, respectively, in good yield.

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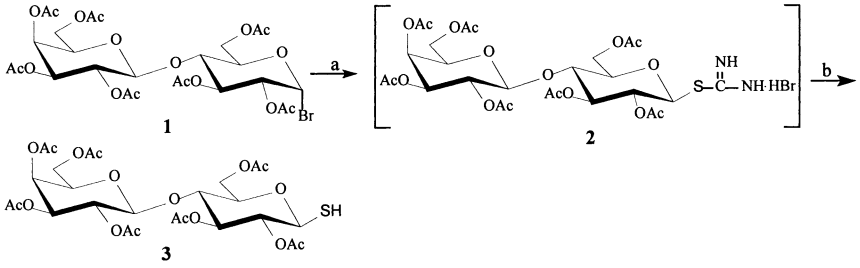
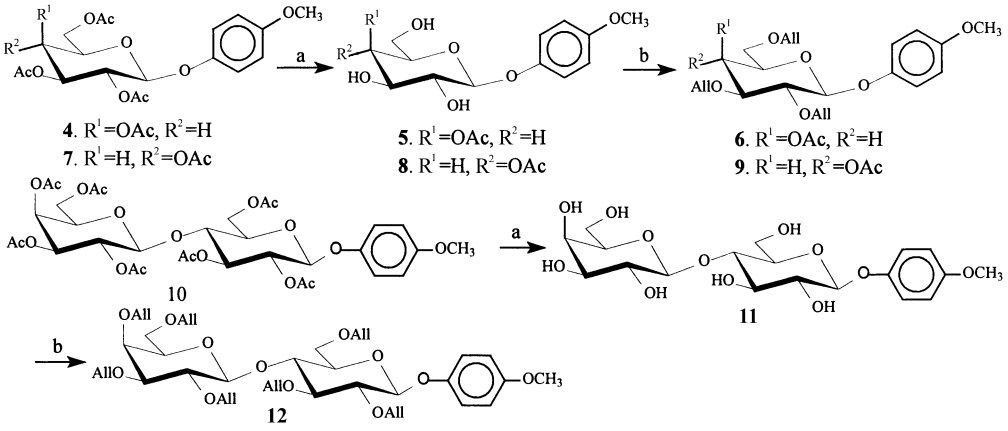
*Synthesis of the free lactoside cluster target compounds (***I**, **II**, and **III**).—Free-radical additions were initiated mostly by exposure to UV radiation or by the addition of chemical initiators. The first case requires special apparatus and undesirable byproducts were formed in the second.[17] We chose a peroxide (*o*-nitroperoxybenzoic acid) as the chain-reaction initiator. The methanolic reaction mixture was thoroughly degassed by a stream of argon and then heated to the decomposition temperature of the catalyst, and boiled under reflux for 8 h. TLC indicated almost complete conversion into **13**, **14**, or **15** when the concentration of **6**, **9**, and **12** in the reaction mixture was about 5 mM. At lower concentrations "under substitution" of **6**, **9**, and **12** occurs; if the concentration of the reactants is too high, then the major product of the reaction is the disulfide formed by dimerization of two molecules of **3**.[18–20]

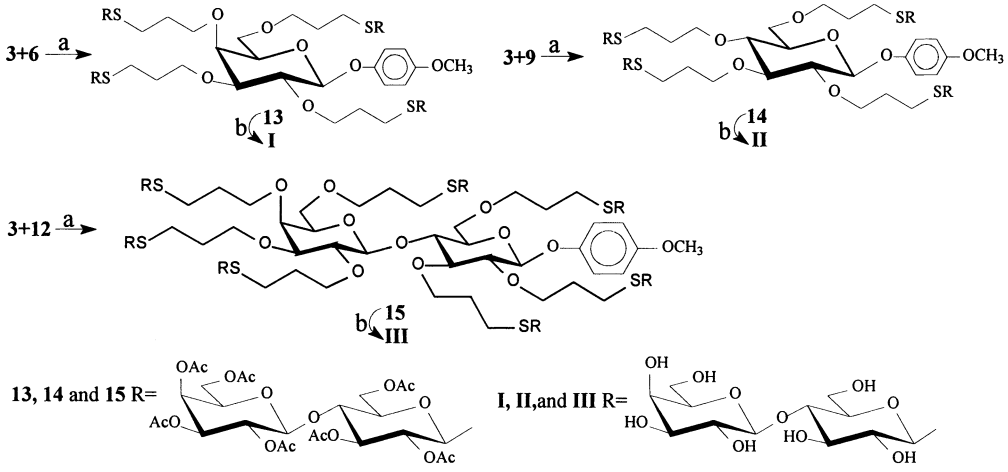
The acetyl-protected compounds **13**, **14**, and **15** were deacetylated to afford the deprotected clusters (**I**, **II**, and **III**) almost quantitatively (Scheme 3).



Scheme 1. (a) Thiourea, acetone, reflux, 30 min. (b) $Na_2S_2O_5$, $CHC1_3$–H_2O, reflux, 30 min. 57.8% (two steps).



Scheme 2. (a) $NaOCH_3$, CH_3OH, ion-exchange resin (H^+); (b) allyl bromide, NaH, DMF, rt.



Scheme 3. (a) CH_3OH, Ar, *o*-nitroperoxybenzoic acid, reflux; (b) $NaOCH_3$, CH_3OH, ion-exchange resin (H^+).

Structural characterizations of the clusters.—The ^{1}H NMR spectra of the clusters are characterized by a number of overlapping peaks due to many magnetically similar CH_2 and CH groups on each molecule. Assignment of the broad-band spectra (especially the sugar ring) is very difficult. The decoupled ^{13}C NMR spectra shared similar features of the ^{1}H NMR spectra. Some of the C signals were difficult to detect because of their relatively small intensities in the higher molecular-weight derivatives.

The elemental analyses of all compounds were in good agreement with theory.

MALDITOF–MS is the best way to confirm if the product assignment is correct. The spectra of **15** obtained in the positive-ion mode indicated two peaks: m/z 5250.8 and 5276.7, which are smaller than the calculated value (5295.0). It was assumed that the relatively high laser energy (0.56 μJ) promoted deacetylation in the presence of the acidic matrix (2,5-dihydroxybenzoic acid) and water. The two peaks (5250.8 and 5276.7) can be assigned as $[M - Ac + 2H]^+$ and $[M - Ac + H + Na]^+$ within the scope of instrumental error.

The anti-metastatic activity of these clusters on tumor cells will be reported in detail elsewhere.

3. Experimental

General methods.—Solvents were purified conventionally. Melting points are uncorrected. NMR spectra were recorded with Varian VXR-300 and Jeol-300 spectrometers. Mass spectra were recorded with an LDI-1700 spectrometer (MALDITOF). Optical rotations were measured using an Optical Activity AA-10R automatic polarimeter. Elemental analyses were performed with a Perkin–Elmer 240C instrument. TLC was performed on Silica gel GF_{254} plates (Hai Yang Chemical Factory, Qingdao, Shandong, PR China) with detection by quenching of UV fluorescence and by spraying with 5% H_2SO_4. Column chromatography was performed on Silica Gel H (10–40 μm, Hai Yang Chemical Factory, Qingdao, Shandong, PR China).

Typical methods for preparation of compounds **6**, **9**, *and* **12**.—To a solution of **5**, **8**, or **11** in anhyd DMF, NaH (60%) was added (1.2 equiv per OH). The mixture was stirred at rt for 15 min, and then allyl bromide (1.5 equiv per OH) was added dropwise. The reaction was completed after 2 h, as indicated by TLC. Drops of MeOH were added to decompose excess NaH, and then the mixture was diluted with toluene and washed with brine. The extracts were dried (Na_2SO_4) and evaporated in vacuo, and the residue chromatographed to give the desired **6**, **9**, and **12** in good yields.

p-*Methoxyphenyl 2,3,4,6-tetra*-O-*allyl*-β-D-*galactopyranoside* (**6**).—Compound **6** (5.62 g, 87.1%) was obtained as white needles; mp 70–71 °C; $[\alpha]_D^{25}$ −23.0° (*c* 1.13, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.99 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.79 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.99–5.85 (m, 4 H, CH_2=C*H*CH_2O), 5.30–5.12 (m, 8 H, C*H*$_2$=CHCH_2O), 4.74 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.42–4.00 (m, 8 H, CH_2=CHC*H*$_2$O), 3.82 (m, 2 H, H-2, H-3), 3.77 (s, 1 H, OCH_3), 3.68 (m, 1 H, H-5) 3.60 (m, 2 H, H-6a,6b), 3.40 (dd, 1 H, *J* 3.3, *J* 6.3 Hz, H-4); ^{13}C NMR ($CDCl_3$): δ 155.2, 151.6 ($C_6H_4OCH_3$), 135.5, 135.3, 135.0, 134.5 (CH_2=*C*HCH_2O), 118.6, 117.2, 116.8, 116.6, 114.5 ($C_6H_4OCH_3$, *C*H$_2$=CHCH_2O), 103.2 (C-1), 81.2 (C-2), 79.0; 74.0, 73.9, 73.6, 73.3 (CH_2=CH*C*H$_2$O), 72.5, 71.9, 68.5 (C-6), 55.7 (OCH_3); MALDITOF–MS: Calcd for $C_{25}H_{34}O_7$: m/z 446.5. Found: m/z $[M + Na]^+$ 469.6, $[M + K]^+$ 485.5. Anal. Calcd for $C_{25}H_{34}O_7$: C, 67.24; H, 6.67. Found: C, 67.16; H, 6.50.

p-*Methoxyphenyl 2,3,4,6-tetra*-O-*allyl*-β-D-*glucopyranoside* (**9**).—Compound **9** (4.00 g, 85.3%) was obtained as a syrup; $[\alpha]_D^{25}$ −18.9° (*c* 2.65, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.99 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.80 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.02–5.85 (m, 4 H, CH_2=C*H*CH_2O), 5.32–5.15 (m, 8 H, C*H*$_2$=CHCH_2O), 4.74 (d, 1 H, $J_{1,2}$ 7.2 Hz, H-1), 4.48–4.01 (m, 8 H, CH_2=CHC*H*$_2$O), 3.77 (s, 1 H, OCH_3), 3.72 (m, 1 H, H-2), 3.62 (dd, *J* 2.7, *J* 3.9 Hz, H-4), 3.45 (br, 4 H, H-3,5,6a,6b); ^{13}C NMR ($CDCl_3$): δ 155.3, 151.6 ($C_6H_4OCH_3$), 135.2, 135.0, 134.8, 134.7 (CH_2=*C*HCH_2O), 118.4 (2 C), 116.9, 116.7, 116.6, 114.5 ($C_6H_4OCH_3$, *C*H$_2$=CHCH_2O), 102.7 (C-1), 84.1, 81.4; 75.0, 74.4, 73.8, 73.7 (CH_2=CH*C*H$_2$O), 72.4, 68.9 (C-6), 55.6 (OCH_3); MALDITOF–MS: Calcd for $C_{25}H_{34}O_7$: m/z 446.5. Found: m/z $[M + Na]^+$ 469.6, $[M + K]^+$ 485.5. Anal. Calcd for $C_{25}H_{34}O_7$: C, 67.24; H, 6.67. Found: C, 67.40; H, 6.45.

p-*Methoxyphenyl 2,3,6,2′,3′,4′,6′-hepta*-O-*allyl*-β-*lactoside* (**12**).—Compound **12** (5.97 g, 79.1%) was obtained as white needles; mp 75–76 °C; $[\alpha]_D^{25}$ −19.6° (*c* 1.43, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.99 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.79 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.02–5.84 (m, 8 H, CH_2=C*H*CH_2O), 5.34–5.10 (m, 16 H, C*H*$_2$=CHCH_2O), 4.74 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.48–3.95 (m, 16 H, CH_2=CHC*H*$_2$O), 3.78 (m, 4 H), 3.76 (s, 3 H, OCH_3), 3.64–3.44 (m, 8 H,), 3.30 (dd, 1 H, *J* 3.3, *J* 3.0 Hz, H-4); ^{13}C NMR ($CDCl_3$): δ 155.2, 151.8 ($C_6H_4OCH_3$), 136.0, 135.7, 135.4, 135.3, 135.0, 134.6 (CH_2=*C*HCH_2O), 118.5, 117.2, 116.6, 116.4, 116.0, 115.8, 114.5 ($C_6H_4OCH_3$, *C*H$_2$=CHCH_2O), 103.1, 102.7 (C-1,1′), 83.1, 82.1, 81.3, 79.5; 75.3, 74.3, 73.9, 73.8, 73.7, 73.1, 72.9, 71.5 (CH_2=CH*C*H$_2$O), 68.5, 68.0 (C-6,6′), 55.7 (OCH_3); MALDITOF–MS: Calcd for $C_{40}H_{56}O_{12}$: m/z 728.9. Found: m/z $[M + Na]^+$ 750.9, $[M + K]^+$ 767.4. Anal. Calcd for $C_{40}H_{56}O_{12}$: C, 65.92; H, 7.74. Found: C, 65.76; H, 7.56.

Typical method for preparation of clusters **13**, **14**, *and* **15**.—The thiol **3** (2 equiv per allyl group) and **6** (**9** or **12**, all at 5 mM) were dissolved in abs MeOH. A stream of Ar was bubbled through the solution for 30 min to thoroughly degas it. The solution, kept under an atmosphere of Ar, was treated with *o*-nitroperoxybenzoic acid (0.1 equiv per allyl group) under reflux until the reaction was complete (8 h). The mixture was diluted with EtOAc, washed with aq $NaHCO_3$, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography to afford the product.

p-*Methoxyphenyl 2,3,4,6-tetra*-O-*[3-(hepta*-O-*acetyl-β-lactosylthio)propyl]-β*-D-*galactopyranoside* (**13**).—Compound **13** (180 mg, 58.8%) was obtained as a foam; $[\alpha]_D^{25}$ −7.5° (*c* 3.48, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.93 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.79 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.31 (m, 4 H), 5.17–4.84 (m, 16 H), 4.43 (m, 14 H), 4.04 (m, 14 H), 3.85–3.77, 3.72–3.58 (m, 15 H), 3.74 (s, 3 H, OCH_3), 3.52 (br, 8 H, $OCH_2CH_2CH_2S$), 2.67 (br, 8 H, $OCH_2CH_2CH_2S$), 2.13, 2.11, 2.07, 2.06, 2.05, 2.04, 2.02, 2.01, 1.93 (∼84 H, Ac), 1.82 (br, 8 H, $OCH_2CH_2CH_2S$); ^{13}C NMR ($CDCl_3$): δ 170.7, 170.6, 170.5, 170.4, 170.0, 169.4 (Ac), 155.5, 151.8, 118.4, 114.9 ($C_6H_4OCH_3$), 101.5 (O-anomeric C), 84.2, 77.8, 77.6 (S-anomeric C) 74.2, 71.8, 71.0, 70.9, 70.8, 69.5, 67.0, 62.6, 61.1; 56.0 (OCH_3), 31.3, 30.8, 30.0 ($OCH_2CH_2CH_2S$), 27.8, 27.7 ($OCH_2CH_2CH_2S$), 21.3, 21.2, 21.1, 21.0, 20.1 (Ac); MALDITOF–MS: Calcd for $C_{129}H_{178}O_{75}S_4$: *m*/*z* 3055.7. Found: *m*/*z* $[M+Na]^+$ 3074.6, $[M+K]^+$ 3091.1. Anal. Calcd for $C_{129}H_{178}O_{75}S_4$: C, 50.68; H, 5.87. Found: C, 50.96; H, 5.58.

p-*Methoxyphenyl 2,3,4,6-tetra*-O-*[3-(hepta*-O-*acetyl-β-lactosylthio)propyl]-β*-D-*glucopyranoside* (**14**).—Compound **14** (200 mg, 65.4%) was obtained as a foam; $[\alpha]_D^{25}$ −21.1° (*c* 0.38, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.93 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.80 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.32 (m, 4 H), 5.21–4.88 (m, 16 H), 4.45 (m, 14 H), 4.05 (m, 14 H), 3.86 (br), 3.63 (m, 15 H), 3.75 (s, 3 H, OCH_3), 3.52 (br, 8 H, $CH_2CH_2CH_2S$), 2.69 (br, 8 H, $CH_2CH_2CH_2S$), 2.32, 2.14, 2.12, 2.08, 2.05, 2.03, 2.02, 2.00, 1.94 (∼84 H, Ac), 1.82 (br, 8 H, $CH_2CH_2CH_2S$); ^{13}C NMR ($CDCl_3$): δ 170.3, 170.1, 170.0, 169.9, 169.7, 169.1 (Ac), 155.2, 151.3, 118.0, 114.5 ($C_6H_4OCH_3$), 101.1 (O-anomeric C), 84.7, 83.8, 83.6, 83.5, 82.0 (S-anomeric C), 77.9, 77.2, 76.2, 76.0, 73.8, 71.6, 71.1, 71.0, 70.9, 70.8, 70.6, 70.4, 70.1, 69.8, 69.7, 69.6, 69.0, 66.6, 62.2, 60.7; 55.6 (OCH_3), 30.5, 30.1, 29.7 ($OCH_2CH_2CH_2S$), 27.6, 27.3, 27.1 ($OCH_2CH_2CH_2S$), 21.0, 20.9, 20.8, 20.6, 20.5 (Ac); MALDITOF–MS: Calcd for $C_{129}H_{178}O_{75}S_4$: *m*/*z* 3055.7. Found: *m*/*z* $[M+Na]^+$ 3076.3. Anal. Calcd for $C_{129}H_{178}O_{75}S_4$: C, 50.68; H, 5.87. Found: C, 50.88; H, 5.74.

p-*Methoxyphenyl 2,3,6,2′,3′,4′,6′-hepta*-O-*[3-(hepta*-O-*acetyl-β-lactosylthio)propyl]-β-lactoside* (**15**).—Compound **15** (220 mg, 46.5%) was obtained as a foam; $[\alpha]_D^{25}$ +8.2° (*c* 0.98, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 6.93 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.79 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.31 (m), 5.17–4.87 (m), 4.47 (br), 4.06 (br), 3.87 (br), 3.64 (br) (∼112 H), 3.75 (s, 3 H, OCH_3), 3.48 (br, 14 H, $OCH_2CH_2CH_2S$), 2.68 (br, 14 H, $OCH_2CH_2CH_2S$), 2.12, 2.08, 2.02, 1.93, 1.81 (∼147 H, Ac), 1.81 (br, 14 H, $OCH_2CH_2CH_2S$); ^{13}C NMR ($CDCl_3$): δ 170.3, 170.1, 169.7, 169.1 (Ac), 155.2, 151.3, 118.0, 114.5 ($C_6H_4OCH_3$), 101.0 (O-anomeric C), 83.7 (S-anomeric C), 76.2, 73.8, 70.9, 70.6, 69.1, 66.6, 62.2, 60.7; 55.6 (OCH_3), 30.0 ($OCH_2CH_2CH_2S$), 27.5 ($OCH_2CH_2CH_2S$), 20.8, 20.6, 20.5 (Ac); MALDITOF–MS: Calcd for $C_{222}H_{308}O_{131}S_7$: *m*/*z* 5295.0. Found: *m*/*z* $[M-Ac+2H]^+$ 5250.8, $[M-Ac+H+Na]^+$ 5276.7. Anal. Calcd for $C_{222}H_{308}O_{131}S_7$: C, 50.36; H, 5.86. Found: C, 50.20; H, 5.65.

Typical method for the preparation of O-*deprotected clusters* **I**, **II**, *and* **III**.—To a solution of **13** (**14** or **15**) in abs MeOH, a catalytic amount of $NaOCH_3$ was added. The mixture was stirred at rt for 5 h, and then water was added until the cloudy solution became clear again. The solution was neutralized with cation-exchange resin (H^+). The resin was filtered off and washed with water, and the combined filtrate and washings were evaporated in vacuo to afford the target clusters quantitatively as white foams.

p-*Methoxyphenyl 2,3,4,6-tetra*-O-*[3-(β-lactosylthio)propyl]-β*-D-*galactopyranoside* (**I**).—$[\alpha]_D^{25}$ +93.7° (*c* 1.26, D_2O); ^{1}H NMR (D_2O): δ 6.92 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.82 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 4.39 (m, 2 H), 4.26 (m, 6 H), 3.74 (s, 3 H, OCH_3), 3.64–3.34 (m, ∼55 H), 3.19 (m, 8 H, $OCH_2CH_2CH_2S$), 2.64 (br, 8 H, $OCH_2CH_2CH_2S$), 1.79 (br, 8 H, $OCH_2CH_2CH_2S$); ^{13}C NMR (D_2O): δ 157.3, 153.5, 120.7, 117.8 ($C_6H_4OCH_3$), 105.5 (O-anomeric C), 88.0, 87.9, 86.3 (S-anomeric C), 81.3, 78.4, 78.0, 78.0, 76.4, 75.2, 75.1, 75.0, 74.7, 74.5, 74.4, 73.7, 73.6, 72.2, 72.0, 72.1, 71.4, 71.2, 63.7, 62.9, 62.8 (3 C), 62.5; 58.5 (OCH_3), 32.9, 32.7, 32.6, 31.9 ($OCH_2CH_2CH_2S$), 29.5 (2 C), 29.4 (2 C), 29.3 ($OCH_2CH_2CH_2S$); MALDITOF–MS: Calcd for $C_{73}H_{122}O_{47}S_4$: *m*/*z* 1878.6. Found: *m*/*z* $[M+Na]^+$ 1901.8. Anal. Calcd for $C_{73}H_{122}O_{47}S_4$: C, 46.67; H, 6.55. Found: C, 47.00; H, 6.88.

p-*Methoxyphenyl 2,3,4,6-tetra*-O-*[3-(β-lactosylthio)propyl]-β*-D-*glucopyranoside* (**II**).—$[\alpha]_D^{25}$ −100.0° (*c* 0.80, D_2O); ^{1}H NMR (D_2O): δ 6.92 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.82 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 4.40 (m, 2 H), 4.25 (br, 6 H), 3.74 (s, 3 H, OCH_3), 3.65–3.34 (m, ∼55 H), 3.20 (br, 8 H, $OCH_2CH_2CH_2S$), 2.67 (br, 8 H, $OCH_2CH_2CH_2S$), 1.77 (br, 8 H, $OCH_2CH_2CH_2S$); ^{13}C NMR (D_2O): δ 157.3, 153.6, 120.8, 117.8 ($C_6H_4OCH_3$), 105.5 (O-anomeric C), 88.0 (S-anomeric C), 81.6, 81.3, 81.0, 78.4, 78.0, 76.2, 75.2, 75.0, 74.7,

74.2, 73.6, 72.2, 72.0, 71.5, 71.2, 63.7, 62.9, 62.5; 58.5 (OCH_3), 32.6, 32.3, 32.0 ($OCH_2CH_2CH_2S$), 29.4 ($OCH_2CH_2CH_2S$); MALDITOF–MS: Calcd for $C_{73}H_{122}O_{47}S_4$: m/z 1878.6. Found: m/z $[M+Na]^+$ 1901.2. Anal. Calcd for $C_{73}H_{122}O_{47}S_4$: C, 46.67; H, 6.55. Found: C, 46.44; H, 6.40.

p-*Methoxyphenyl 2,3,4,2′,3′,4′,6′-hepta*-O-*(3-β-lactosylthio)propyl-β-lactoside* (**III**).—$[\alpha]_D^{25}$ +106.0° (*c* 1.17, D_2O); ^1H NMR (D_2O): δ 6.94 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.82 (d, 2 H, *J* 9.0 Hz, $C_6H_4OCH_3$), 4.40 (m, 4 H), 4.26 (br, 10 H), 3.74 (s, 3 H, OCH_3), 3.97–3.33 (m, ~98 H), 3.20 (br, 14 H, $OCH_2CH_2CH_2S$), 2.68 (br, 14 H, $OCH_2CH_2CH_2S$), 1.78 (br, 8 H, $OCH_2CH_2CH_2S$); ^{13}C NMR (D_2O): δ 157.3, 153.6, 120.6, 117.8 ($C_6H_4OCH_3$), 105.8 (O-anomeric C), 91.9, 88.1, 88.0 (2 C) (S-anomeric C), 81.7, 81.3, 80.9, 78.5, 78.2, 78.0, 75.2, 74.8, 74.7, 73.9, 73.4, 71.2, 63.7, 63.0, 62.8, 62.6; 58.5 (OCH_3), 32.9, 32.8 ($OCH_2CH_2CH_2S$), 29.5 ($OCH_2CH_2CH_2S$); MALDI-TOF–MS: Calcd for $C_{124}H_{210}O_{82}S_7$: m/z 3235.0. Found: m/z $[M+Na]^+$ 3256.7. Anal. Calcd for $C_{124}H_{210}O_{82}S_7$: C, 46.04; H, 6.54. Found: C, 46.36; H, 6.77.

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