Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 12310–12316

Oligosaccharides through reactivity tuning: convergent synthesis of the trisaccharides of the steroid glycoside Sokodoside B isolated from marine sponge *Erylus placenta*☆

Somnath Dasgupta,[a] Kausikisankar Pramanik[b] and Balaram Mukhopadhyay[a,*]

[a]*Medicinal and Process Chemistry Division, Central Drug Research Institute, Chattar Manzil Palace, Lucknow 226001, Uttar Pradesh, India*
[b]*Department of Chemistry, Inorganic Chemistry Section, Jadavpur University, Jadavpur, Kolkata 700032, West Bengal, India*

Received 10 July 2007; revised 11 September 2007; accepted 27 September 2007
Available online 29 September 2007

Dedicated to Professor Yashwant D. Vankar, Chemistry Department, Indian Institute of Technology, Kanpur, India

Abstract—Chemical synthesis of the trisaccharide of the steroid glycoside Sokodoside B isolated from *Erylus placenta* is reported. Stereoselective, high-yielding glycosylation strategies through thioglycoside activation using H_2SO_4 immobilized on silica in conjunction with *N*-iodosuccinimide are used for better results. A late stage TEMPO-mediated oxidation was performed for the formation of required uronic acid moiety. An analog of the target trisaccharide is also prepared by using a bis-glycosylation approach.

1. Introduction

Marine sponge derived triterpene glycosides have earned a great deal of interest in past years for their biological activities that include antimicrobial, cytotoxic, and growth inhibitory. Thus, considerable effort has been paid to the isolation and characterization of this unique class of secondary metabolites. As a result various steroid glycosides with different biodynamic characters have been reported from taxonomically diverse marine sponges such as Niphatidae,[1] Pachastrellidae,[2] Ancorinidae,[3,4] Mycalidae,[5] and Raspalidae.[6] Similar to that of saponins, the glycosides attached to the steroid aglycon are highly important for the biological activities they exert. It is believed that the glycosylation occurs at a late stage of the biosynthetic pathway of these natural products. However, exact order of events and the involvement of characteristic glycosyl transferases responsible are still ambiguous. Therefore, chemical synthesis of the oligosaccharide fragments related to marine sponge derived steroid glycosides will be highly relevant when detailed elucidation of the biosynthetic pathway of the total structure is concerned.

During the course of their screening for growth inhibitory activities against genetically modified yeasts, Fusetani et al.[7] have found and characterized a novel steroid glycoside, Sokodoside B, from the marine sponge *Erylus placenta* collected off Hachijo Island. Sokodoside B exhibited a broad spectrum of growth inhibitory activities against several strains of yeasts and fungus. In continuation to our effort toward the syntheses of biodynamic oligosaccharides, here we report a convergent route for the synthesis of the trisaccharide (**1**, Fig. 1) of Sokodoside B involving a TEMPO-mediated oxidation at a late stage[8] of the total synthesis. Once the target trisaccharide has been made through one-to-one glycosylation approach, we then achieved the same target using reactivity tuning approach by exploiting the reactivity difference between 2- and 3-positions of arabinose moiety. Synthesis of an analog (**2**, Fig. 1) of the target structure is also reported by using a bis-glycosylation approach.

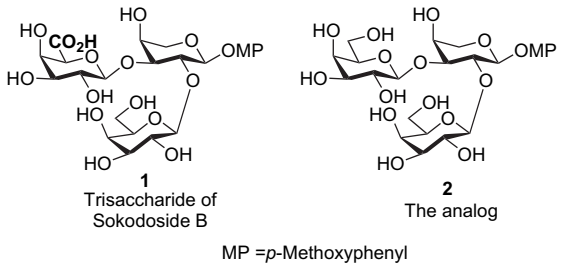


Figure 1. Target structure of the trisaccharide of Sokodoside B isolated from marine sponge *Erylus placenta* and its analog.

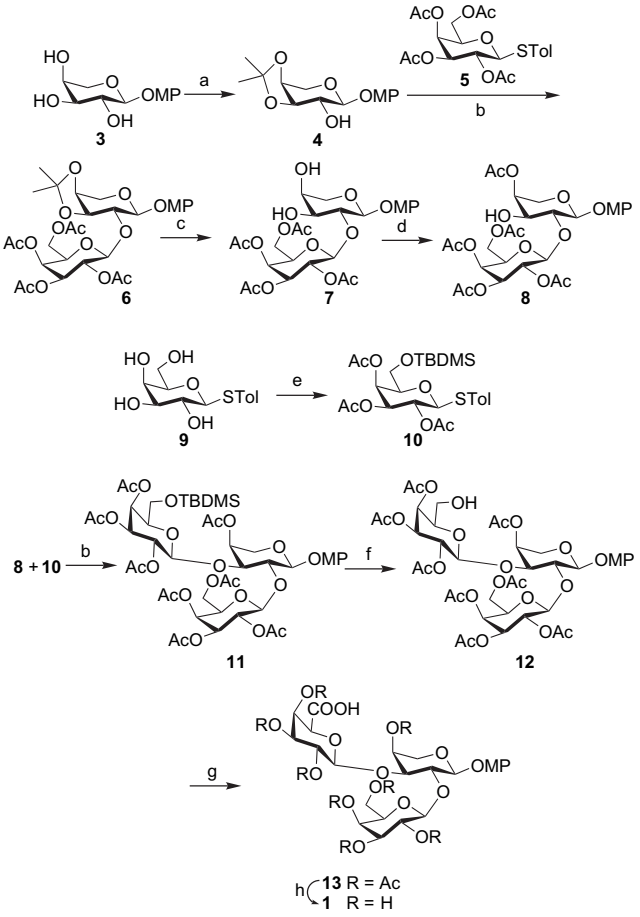
☆ CDRI communication no. 7270.
* Corresponding author. E-mail: sugarnet73@hotmail.com

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.09.072

2. Results and discussion

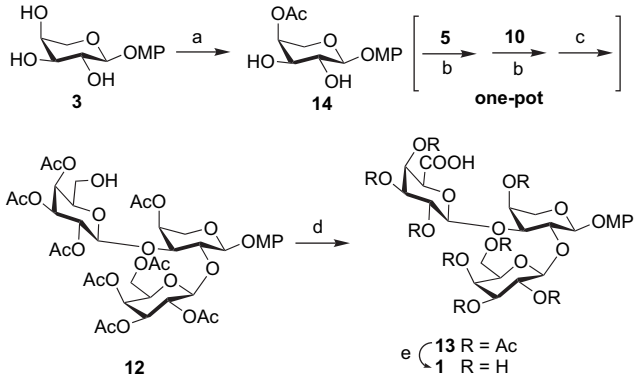
2.1. Synthesis of the trisaccharide (1) of Sokodoside B

Synthesis of the trisaccharide commenced with known *p*-methoxyphenyl α-L-arabinopyranoside (**3**). *p*-Methoxyphenyl group at the reducing end was chosen since selective deprotection at the target trisaccharide stage is possible to prepare glycoconjugates for biological screening. Arabinoside **3** was converted to its 3,4-*O*-isopropylidene derivative **4** using 2,2-dimethoxy propane and acetone in the presence of 10-camphorsulfonic acid.[9] Then compound **4** was coupled with known *p*-tolyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**5**) using *N*-iodosuccinimide in the presence of H_2SO_4–silica[10] to afford disaccharide **6** in 89% yield. Use of H_2SO_4–silica as the catalyst for NIS promoted thioglycoside activation instead of using corrosive TfOH or TMSOTf was proved to be a better choice as it is much easier to handle. Removal of isopropylidene acetal by 80% AcOH at 80 °C[11] followed by orthoesterification and rearrangement furnished the disaccharide acceptor **8** in 85% yield. In a separate experiment, known thiogalactoside **9** was treated with TBDMS-Cl in pyridine[12] followed by Ac_2O to afford *p*-tolyl 2,3,4-tri-*O*-acetyl-6-*O*-(*tert*-butyl dimethylsilyl)-1-thio-β-D-galactopyranoside (**10**) in 81% yield. Glycosylation between disaccharide acceptor **8** and donor **10** using NIS in the presence of H_2SO_4–silica furnished the protected trisaccharide **11** in 83% yield. The TBDMS group was then removed selectively using 1 M Bu_4NF in THF[13] using equimolar amount of AcOH in the reaction media to prevent the migration of the 4-*O*-acetyl group to 6-position. Extraction and purification of the crude material afforded the trisaccharide **12** in 78% yield. Oxidation of the primary OH group to obtain the required uronic acid moiety, TEMPO-mediated phase-transfer oxidation process, has been used as reported by Huang et al.[14] Among other methods available in the literature,[15] this protocol was particularly of interest as the phase-transfer condition is favorable for a blocked oligosaccharide. The reaction was satisfactory and afforded the corresponding uronic acid derivative **13** in 75% yield. Global deprotection of the acetyl groups using Zemplén conditions furnished the target trisaccharide **1** in 87% yield (Scheme 1).



Scheme 1. Synthesis of trisaccharide **1** through conventional one-to-one glycosylation approach. *Reagents and conditions*: (a) 2,2-DMP, acetone, CSA, rt, 30 min; (b) NIS, H_2SO_4–silica, MS 4 Å, CH_2Cl_2, −40 °C, 1 h; (c) 80% AcOH, 80 °C, 2 h; (d) (i) trimethyl orthoacetate, CSA, CH_3CN, 1 h; (ii) 80% AcOH, rt, 45 min; (e) (i) TBDMS-Cl, Py, 4 h; (ii) Ac_2O, 2 h; (f) Bu_4NF–THF, AcOH, 0 °C–rt, 16 h; (g) TEMPO, NaOCl, $NaOCl_2$, CH_2Cl_2; (h) NaOMe, MeOH, rt, 3 h.

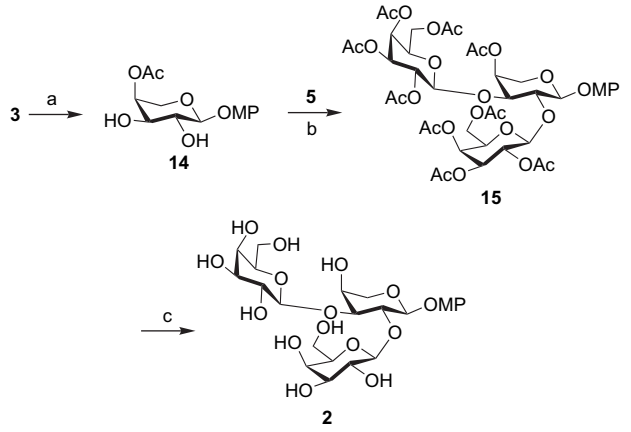
During the course of the glycosylation steps for the synthesis of trisaccharide **1**, we observed that low temperature (−30 to −40 °C) is necessary for clean conversion. At higher temperature (greater than −10 °C) partial loss of TBDMS group was observed. Taking the advantage of this observation and anticipating the reactivity difference among 2- and 3-positions of arabinose moiety, we have targeted one-pot sequential glycosylation approach. Thus, *p*-methoxyphenyl 4-*O*-acetyl-α-L-arabinopyranoside (**14**) was prepared from **3** by making the corresponding 3,4-orthoester derivative using trimethyl orthoacetate and then rearrangement by 80% AcOH at room temperature. The acceptor diol (**14**) was first coupled with donor **10** followed by addition of the second donor **5**. The sequential glycosylations were performed at −40 °C using NIS and H_2SO_4–silica and afforded the same trisaccharide as obtained from the previous approach. After complete glycosylation, the temperature of the reaction mixture was raised to room temperature during 1 h. To our satisfaction, the required removal of the TBDMS group was achieved cleanly to afford the trisaccharide **12** ready for oxidation. Similar to the previous approach, the primary OH group was oxidized using Huang's condition and global deprotection furnished the target trisaccharide **1** (Scheme 2).



Scheme 2. Synthesis of trisaccharide **1** through sequential one-pot glycosylation approach using reactivity tuning. *Reagents and conditions*: (a) (i) trimethyl orthoacetate, CSA, CH_3CN, 1 h; (ii) 80% AcOH, rt, 45 min; (b) NIS, H_2SO_4–silica, MS 4 Å, CH_2Cl_2, −40 °C, 1 h; (c) temperature raised to 10 °C in 1 h; (d) TEMPO, NaOCl, $NaOCl_2$, CH_2Cl_2; (e) NaOMe, MeOH, rt, 3 h.

2.2. Synthesis of the trisaccharide analog (2) of Sokodoside B

For the analog of Sokodoside B trisaccharide, compound **3** was reacted with trimethyl orthoacetate in the presence of CSA to get the corresponding 3,4-orthoester, which was subsequently rearranged using 80% AcOH at room temperature to afford the diol acceptor **14** in 86% yield. Acceptor diol (**14**) was coupled with two galactose moieties by using 2.5 equiv of the donor **5**. Same NIS promoted activation of thioglycoside donor in the presence of H_2SO_4–silica afforded the bis-glycosylated product **15** in 84% yield. De-O-acetylation using Zemplén condition afforded the target analog **2** in 89% yield as amorphous white powder (Scheme 3).



Scheme 3. Synthesis of trisaccharide **2** using bis-glycosylation approach. *Reagents and conditions*: (a) (i) trimethyl orthoacetate, CSA, CH_3CN, rt, 1 h; (ii) 80% AcOH, rt, 45 min; (b) NIS, H_2SO_4–silica, MS 4 Å, CH_2Cl_2, 10 °C, 1 h; (c) NaOMe, MeOH, rt, 3 h.

3. Conclusion

In conclusion, we have successfully prepared the trisaccharide of the steroid glycoside Sokodoside B using conventional one-to-one approach and also through one-pot sequential glycosylation using reactivity tuning strategy. TEMPO-mediated phase-transfer oxidation was performed efficiently at a late stage of the total synthesis. An analog of the concerned trisaccharide has also been synthesized in very good yield using a bis-glycosylation approach. The choice of the *p*-methoxyphenyl group as reducing end glycoside in all cases offers further glycoconjugate formation for future biological evaluation of the synthesized oligosaccharides.

4. Experimental

4.1. General methods

All reagents and solvents were dried prior to use according to standard methods.[16] Commercial reagents were used without further purification unless otherwise stated. Analytical TLC was performed on silica gel 60-F_{254} (Merck or Whatman) with detection by fluorescence and/or by charring following immersion in a 10% ethanolic solution of sulfuric acid. An orcinol dip, prepared by careful addition of concentrated sulfuric acid (20 cm^3) to an ice-cold solution of 3,5-dihydroxytoluene (360 mg) in EtOH (150 cm^3) and water (10 cm^3), was used to detect deprotected compounds by charring. Flash chromatography was performed with silica gel 230–400 mesh (Qualigens, India). Optical rotations were measured at the sodium D-line at ambient temperature with a Perkin–Elmer 141 polarimeter. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance spectrometer at 300 and 75 MHz, respectively, using Me_4Si or CH_3OH as internal standard, as appropriate.

Preparation of H_2SO_4–silica: to a slurry of silica gel (10 g, 200–400 mesh) in dry diethyl ether (50 mL) was added commercially available concd H_2SO_4 (1 mL) and shaken for 5 min. Solvents were evaporated under reduced pressure resulting in free flowing H_2SO_4–silica. It was then dried at 110 °C for 3 h and used for the reaction.

4.1.1. *p*-Methoxyphenyl 3,4-*O*-isopropylidene-α-L-arabinopyranoside (4). To a slurry of compound **3** (3 g, 11.7 mmol) in dry acetone (20 mL) was added 2,2-DMP (1.7 mL, 14 mmol) followed by CSA (15 mg). The mixture was allowed to stir at room temperature for 30 min when the solution became clear and the starting material was completely converted to a faster running spot (R_f 0.6, *n*-hexane–EtOAc; 1:1). The solution was neutralized with Et_3N and the solvents were evaporated in vacuo. The light brown syrupy mass was purified by flash chromatography using 3:1 *n*-hexane–EtOAc as eluent to afford pure compound **4** (3.15 g, 91%) as colorless glass. $[\alpha]_D^{25}$ +102 (*c* 1.0, $CHCl_3$). IR (neat): 2360, 1598, 1373, 1226, 1075 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.93 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.77 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 4.73 (d, 1H, *J* 7.2 Hz, H-1), 4.29–4.26 (m, 1H, H-4), 4.10 (t, 1H, *J* 7.2 Hz, H-2), 4.08 (dd, 1H, *J* 4.5, 7.2 Hz, H-3), 3.86 (dd, 1H, *J* 2.1, 12.9 Hz, H-5a), 3.82 (dd, 1H, *J* 4.2, 12.9 Hz, H-5b), 3.75 (s, 3H, $C_6H_4OCH_3$), 2.94 (br s, 1H, O*H*), 1.54 (s, 3H, isopropylidene-CH_3), 1.36 (s, 3H, isopropylidene-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 148.8, 136.7, 118.7, 114.7 (ArC), 110.2 (isopropylidene-*C*), 101.5 (C-1), 77.9, 72.9, 72.4, 62.7 (C-5), 55.5 ($C_6H_4OCH_3$), 27.8, 25.8 (2×isopropylidene-C). HRMS Calcd for $C_{15}H_{24}O_6N$ ($M+NH_4$): 314.1604; found 314.1601.

4.1.2. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→2)-3,4-*O*-isopropylidene-α-L-arabinopyranoside (6). A mixture of compound **4** (1 g, 3.4 mmol), compound **5** (2 g, 4.8 mmol), and MS 4 Å (2 g) in dry CH_2Cl_2 (25 mL) was stirred under nitrogen for 1 h. After addition of NIS (1.4 g, 6.2 mmol), the mixture was cooled to −40 °C followed by addition of H_2SO_4–silica (30 mg) and the mixture was allowed to stir at the same temperature for 1 h when the acceptor **4** was completely consumed (R_f 0.3, *n*-hexane–EtOAc; 2:1). The mixture was filtered through a pad of Celite and the filtrate was washed successively with $Na_2S_2O_3$ (2×30 mL), $NaHCO_3$ (2×30 mL), and brine (30 mL). The organic layer was collected, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by flash chromatography using 2:1 *n*-hexane–EtOAc as eluent to afford the disaccharide **6** (1.9 g, 89%) as colorless foam. $[\alpha]_D^{25}$ +106 (*c* 1.1, $CHCl_3$). IR (KBr): 1753, 1725, 1637, 1605, 1367, 1229, 1045 cm^{-1}; ^1H NMR

(300 MHz, $CDCl_3$) δ: 6.94 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 6.78 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 5.32 (m, 1H, H-4′), 5.20 (dd, 1H, J 8.1, 10.5 Hz, H-2′), 5.04 (d, 1H, J 7.8 Hz, H-1), 5.01 (dd, 1H, J 4.2, 10.5 Hz, H-3′), 4.75 (d, 1H, J 8.1 Hz, H-1′), 4.32 (m, 1H, H-4), 4.11 (t, 1H, J 7.8 Hz, H-2), 4.02–3.80 (m, 5H, H-5a, H-5b, H-5′, H-6a′, H-6b′), 3.73 (s, 3H, $C_6H_4OCH_3$), 3.67 (dd, 1H, J 3.3, 7.8 Hz, H-3), 2.10, 2.07, 1.96, 1.88 (4s, 12H, 4×$COCH_3$), 1.51 (s, 3H, isopropylidene-CH_3), 1.23 (s, 3H, isopropylidene-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.4, 170.2 (2), 169.7 (4×$COCH_3$), 155.6, 151.2, 118.5, 114.9 (ArC), 102.9 (C-1′), 100.4 (C-1), 83.2, 76.7, 72.2, 71.1 (2C), 69.5, 67.1, 62.4, 61.0, 55.9 ($C_6H_4OCH_3$), 28.1, 26.0 (2×isopropylidene-C), 21.2, 21.0, 20.9, 20.8 (4×$COCH_3$). HRMS Calcd for $C_{29}H_{42}O_{15}N$ (M+NH_4): 644.2554; found 644.2551.

4.1.3. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→2)-α-L-arabinopyranoside (7). A solution of compound **6** (1.8 g, 5.4 mmol) in AcOH–H_2O (9:1, 20 mL) was stirred at 80 °C for 2 h when the starting material was completely converted to a slower moving component (TLC). The solvents were evaporated, co-evaporated with toluene, and the crude product was purified by flash chromatography using *n*-hexane–EtOAc (1:1) as eluent to afford pure compound **7** (1.6 g, 96%) as white amorphous powder. $[\alpha]_D^{25}$ +98 (*c* 1.0, $CHCl_3$). IR (KBr): 2933, 2365, 1753, 1594, 1375, 1224, 1047 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.98 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 6.78 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 5.44 (m, 1H, H-4′), 5.17 (dd, 1H, J 8.1, 9.6 Hz, H-2′), 5.04 (dd, 1H, J 3.3, 9.6 Hz, H-3′), 5.02 (d, 1H, J 7.8 Hz, H-1), 4.82 (d, 1H, J 8.1 Hz, H-1′), 4.13–3.86 (m, 5H, H-5′, H-5a, H-5b, H-6a′, H-6b′), 3.82–3.75 (m, 2H, H-2, H-4), 3.74 (s, 3H, $C_6H_4OCH_3$), 3.58 (dd, 1H, J 3.3, 7.8 Hz, H-3), 3.41 (br s, 1H, O*H*), 3.24 (br s, 1H, O*H*), 2.12, 2.07, 1.98, 1.90 (4s, 12H, 4×$COCH_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.0, 169.9 (2C), 169.7 (4×$COCH_3$), 155.2, 150.4, 117.7, 114.5 (ArC), 101.8 (C-1′), 100.0 (C-1), 79.7, 77.2, 70.9, 70.6 (2C), 69.3, 66.9, 66.6, 63.4, 60.6, 55.4 ($C_6H_4OCH_3$), 20.7, 20.6 (2C), 20.5 (4×$COCH_3$). HRMS Calcd for $C_{26}H_{38}O_{15}N$ (M+NH_4): 604.2241; found 604.2243.

4.1.4. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→2)-4-*O*-acetyl-α-L-arabinopyranoside (8). To a solution of compound **7** (1.5 g, 2.6 mmol) in dry CH_3CN (20 mL) were added trimethyl orthoacetate (0.5 mL, 3.9 mmol) and CSA (15 mg), and the solution was stirred at room temperature for 1 h. Then the solution was neutralized with Et_3N and the solvents were evaporated in vacuo. The residue was dissolved in AcOH (80% aq) and stirred at room temperature for 45 min. Solvents were evaporated and co-evaporated with toluene and the resulting crude product was purified by flash chromatography using *n*-hexane–EtOAc (2:1) to furnish the disaccharide acceptor **8** (1.4 g, 85%) as white foam. $[\alpha]_D^{25}$ +101 (*c* 1.1, $CHCl_3$). IR (KBr): 2941, 2372, 1760, 1603, 1383, 1231, 1057 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.95 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 6.80 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 5.34 (m, 1H, H-4′), 5.19 (dd, 1H, J 8.1, 10.5 Hz, H-2′), 5.08–4.96 (m, 3H, H-1, H-3′, H-4), 4.81 (d, 1H, J 8.1 Hz, H-1′), 4.03–3.85 (m, 5H, H-5′, H-5a, H-5b, H-6a′, H-6b′), 3.79 (m, 1H, H-2), 3.73 (s, 3H, $C_6H_4OCH_3$), 3.59 (dd, 1H, J 2.1, 8.1 Hz, H-3), 3.41, 2.98 (br s, H, O*H*), 2.10 (2), 2.08, 1.96, 1.89 (5s, 15H, 5×$COCH_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.8 (2C), 170.6, 170.5, 169.8 (5×$COCH_3$), 155.8, 150.6, 118.1 (2C), 115.0 (2C) (ArC), 102.2 (C-1′), 100.4 (C-1), 79.8, 71.3, 71.1, 69.8, 69.6, 69.3, 67.2, 61.8, 61.2, 56.0 ($C_6H_4OCH_3$), 21.4, 21.2, 21.0, 20.9 (2C) (5×$COCH_3$). HRMS Calcd for $C_{28}H_{40}O_{16}N$ (M+NH_4): 646.2347; found 646.2345.

4.1.5. *p*-Tolyl 2,3,4-tri-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-galactopyranoside (10). To a solution of compound **9** (1.5 g, 5.2 mmol) in dry pyridine (20 mL) was added TBDMS-Cl (1.1 g, 6.8 mmol) and the solution was allowed to stir for 4 h at room temperature. After that, Ac_2O (5 mL) was added and the solution was stirred for an additional 2 h. The solvents were evaporated in vacuo and co-evaporated with toluene to remove traces of pyridine. The residue was purified by flash chromatography using *n*-hexane–EtOAc (5:1) to afford compound **10** (2.2 g, 81%) as colorless glass. $[\alpha]_D^{25}$ +68 (*c* 1.1, $CHCl_3$). IR (neat): 1753, 1375, 1232, 1067, 778 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.38 (d, 2H, $SC_6H_4CH_3$), 7.10 (d, 2H, $SC_6H_4CH_3$), 5.46 (d, 1H, J 3.0 Hz, H-4), 5.20 (t, 1H, J 9.9 Hz, H-2), 5.03 (dd, 1H, J 3.0, 9.9 Hz, H-3), 4.64 (d, 1H, J 9.9 Hz, H-1), 3.71 (m, 2H, H-6a, H-6b), 3.58 (m, 1H, H-5), 2.31 (s, 3H, $SC_6H_4CH_3$), 2.08, 2.06, 1.84 (3s, 9H, 3×$COCH_3$), 0.84 [s, 9H, $C(CH_3)_3$], −0.21, −0.22 [2s, 6H, $Si(CH_3)_2C(CH_3)_3$]. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.0, 168.9, 168.3 (3×$COCH_3$), 137.2, 132.4 (2C), 129.04 (2C), 128.7 (ArC), 86.2 (C-1), 76.6, 71.8, 67.1, 66.8, 60.4 (C-6), 25.3 (3) [$C(CH_3)_3$], 20.6, 20.2, 20.0 (3×$COCH_3$), 17.6 [$C(CH_3)_3$], −5.6, −6.0 [$Si(CH_3)_2$]. HRMS Calcd for $C_{25}H_{42}O_8NSSi$ (M+NH_4): 544.2400; found 544.2402.

4.1.6. *p*-Methoxyphenyl 2,3,4-tri-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl-β-D-galactopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-arabinopyranoside (11). A mixture of compound **8** (1.3 g, 2.1 mmol), compound **10** (1.4 g, 2.7 mmol), and MS 4 Å (2 g) in dry CH_2Cl_2 (25 mL) was stirred under nitrogen for 1 h. NIS (800 mg, 3.5 mmol) was added and the mixture was cooled to −40 °C followed by addition of H_2SO_4–silica (20 mg), and the mixture was allowed stir at the same temperature for 1 h when all acceptor disaccharide **8** was consumed (R_f 0.4, *n*-hexane–EtOAc; 1:1). The mixture was immediately filtered through a pad of Celite and the filtrate was washed successively with $Na_2S_2O_3$ (2×30 mL), $NaHCO_3$ (2×30 mL), and brine (30 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated. The crude product thus obtained was purified by flash chromatography using *n*-hexane–EtOAc (2:1) to get the pure trisaccharide **11** (1.8 g, 83%) as white foam. $[\alpha]_D^{25}$ +91 (*c* 1.0, $CHCl_3$). IR (KBr): 1745, 1387, 1225, 1076, 768 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.93 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 6.80 (d, 2H, J 9.0 Hz, $C_6H_4OCH_3$), 5.43 (d, 1H, J 3.0 Hz, H-4′), 5.32 (d, 1H, J 3.3 Hz, H-4″), 5.23 (d, 1H, J 3.3 Hz, H-4), 5.15 (t, 2H, J 9.0 Hz, H-2′, H-2″), 5.11–5.03 (m, 3H, H-1, H-3′, H-3″), 4.76 (d, 1H, J 7.8 Hz, H-1′), 4.65 (d, 1H, J 7.8 Hz, H-1″), 4.16 (m, 1H, H-3), 3.98 (m, 2H, H-6a′, H-6a″), 3.86–3.74 (m, 3H, H-2, H-5a, H-6b′), 3.79 (s, 3H, $C_6H_4OCH_3$), 3.72–3.55 (m, 3H, H-5′, H-5″, H-6b″), 3.48 (dd, 1H, J 3.3, 11.4 Hz, H-5b), 2.19, 2.15, 2.11, 2.03, 2.02,

1.98, 1.96, 1.94 (8s, 24H, 8×COCH_3), 0.85 [s, 9H, C(CH_3)$_3$], −0.11, −0.12 [2s, 6H, Si(CH_3)$_2$C(CH$_3$)$_3$]. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.1 (2C), 170.0 (2C), 169.4 (2C), 168.9, 168.8 (8×*C*OCH$_3$), 155.1, 149.8, 117.9 (2C), 114.5 (2C) (ArC), 100.7 (C-1′), 100.3 (C-1″), 96.1 (C-1), 78.6, 76.3, 75.7, 73.2, 70.9, 69.4, 68.7, 67.3, 66.8, 66.3, 66.0, 60.2, 60.00, 59.2, 55.3 (C_6H_4OCH_3), 25.7 (3) [C(*C*H$_3$)$_3$], 20.9 (2C), 20.7, 20.6 (2C), 20.5 (2C), 20.4 (8×CO*C*H$_3$), 18.1 [C(*C*H$_3$)$_3$], −5.6, −5.7 [Si(*C*H$_3$)$_2$]. HRMS Calcd for $C_{46}H_{70}O_{24}NSi$ (M+NH$_4$): 1048.4057; found 1048.4055.

4.1.7. *p*-Methoxyphenyl 2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-arabinopyranoside (12). To a stirred solution of compound **11** (1.5 g, 1.45 mmol) in dry THF (20 mL) at 0 °C was added AcOH (93 μL, 1.6 mmol) followed by Bu_4NF (1 N in THF, 7.4 mL) and the solution was allowed to stir at room temperature for 12 h when the starting material was completely converted to a slower moving spot (R_f 0.1, *n*-hexane–EtOAc; 1:2). The solvents were evaporated at temperature <30 °C in vacuo. The crude product was purified by flash chromatography using *n*-hexane–EtOAc (1:1) as eluent to afford pure compound **12** (1.0 g, 78%). $[\alpha]_D^{25}$ +107 (*c* 1.0, $CHCl_3$). IR (neat): 2939, 2373, 1758, 1605, 1386, 1237, 1053 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.96 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.81 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.43 (d, 1H, *J* 3.0 Hz, H-4′), 5.36 (d, 1H, *J* 3.3 Hz, H-4″), 5.26 (d, 1H, *J* 3.3 Hz, H-4), 5.23–5.11 (m, 2H, H-2′, H-2″), 5.05 (dd, 1H, *J* 2.1, 9.3 Hz, H-3′), 5.03 (m, 2H, H-1, H-3″), 4.95 (d, 1H, *J* 7.8 Hz, H-1′), 4.67 (d, 1H, *J* 7.8 Hz, H-1″), 4.29 (m, 1H, H-3), 4.09–3.91 (m, 5H, H-2, H-5a, H-6a′, H-6a″, H-6b′), 3.76 (s, 3H, $C_6H_4OCH_3$), 3.57–3.48 (m, 4H, H-5′, H-5″, H-5b, H-6b″), 3.18 (br s, 1H, O*H*), 2.21, 2.20, 2.16, 2.11, 2.10, 2.03, 1.98, 1.96 (8s, 24H, 8×COCH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 169.8, 169.7 (2C), 169.5 (2C), 169.1 (2C), 168.9 (8×*C*OCH$_3$), 154.8, 149.5, 118.2 (2C), 114.1 (2C) (ArC), 100.3 (C-1′), 100.1 (C-1″), 97.9 (C-1), 78.0, 76.8, 76.4, 75.7, 74.5, 73.8, 73.2, 70.7, 68.8, 68.4, 66.9, 66.4, 62.5, 60.6, 55.0 (C_6H_4OCH_3), 20.9 (2C), 20.4 (2C), 20.2 (2C), 20.1 (2C) (8×CO*C*H$_3$). HRMS Calcd for $C_{40}H_{56}O_{24}N$ (M+NH$_4$): 934.3192; found 934.3193.

4.1.8. *p*-Methoxyphenyl 2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-arabinopyranosiduronic acid (13). To a solution of compound **12** (800 mg, 0.9 mmol) in CH_2Cl_2 (21 mL) and H_2O (4.5 mL) were added aq NaBr (1 M, 480 μL, 0.5 mmol), aq tetrabutylammonium bromide (1 M, 960 μL, 1 mmol), TEMPO (45 mg, 0.3 mmol), and saturated aq $NaHCO_3$ (2.4 mL) at 0 °C. To the resulting mixture, aq NaOCl (2.9 mL) was added and the mixture was allowed to stir for 1.5 h when the temperature was raised from 0 °C to room temperature. At this point TLC showed complete conversion of the starting material to a faster moving spot, presumably the corresponding aldehyde derivative. The mixture was neutralized with 1 N HCl (~250 μL) to keep the pH of the mixture at 6–7. Then *tert*-butanol (13 mL), 2-methyl-but-2-ene (2 M in THF, 27 mL), $NaOCl_2$ (960 mg, 8.8 mmol), and NaH_2PO_4 (765 mg, 6.4 mmol) were added and the mixture was allowed to stir at room temperature for another 4 h when TLC showed complete conversion. The mixture was diluted with saturated NaH_2PO_4 (45 mL) and the product was extracted with EtOAc (3×30 mL). The combined organic layer was dried (Na_2SO_4) and evaporated. The crude product thus obtained was purified by flash chromatography using *n*-hexane–EtOAc (1:4) to neat EtOAc to afford pure compound **13** (610 mg, 75%) as light yellow gel. $[\alpha]_D^{25}$ +86 (*c* 1.1, $CHCl_3$). IR (neat): 2368, 1759, 1603, 1387, 1232, 1049, 738 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.95 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.79 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.40 (d, 1H, *J* 3.0 Hz, H-4′), 5.34 (d, 2H, *J* 3.3 Hz, H-4, H-4″), 5.32–5.19 (m, 3H, H-1, H-2′, H-2″), 5.06 (m, 2H, *J* 2.1, 9.3 Hz, H-3′, H-3″), 4.91 (d, 1H, *J* 7.8 Hz, H-1′), 4.85 (d, 1H, *J* 7.8 Hz, H-1″), 4.38 (m, 1H, H-3), 4.09–4.00 (m, 5H, H-2, H-5′, H-5″, H-6a′, H-6a″), 3.86 (m, 1H, H-5a), 3.75 (s, 3H, $C_6H_4OCH_3$), 3.55 (m, 1H, H-5b), 2.14, 2.13, 2.12, 2.10, 2.03, 2.01, 1.98, 1.94 (8s, 24H, 8×COCH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.9 (*C*OOH), 170.4, 170.0, 169.7 (2C), 169.0 (2C), 169.1, 168.9 (8×*C*OCH$_3$), 155.0, 150.1, 117.8 (2C), 114.5 (2C) (ArC), 100.2 (C-1′), 100.0 (C-1″), 97.7 (C-1), 78.1, 76.6, 76.5, 75.8, 74.7, 73.6, 73.1, 70.9, 68.7, 68.5, 67.0, 66.4, 62.5, 55.4 ($C_6H_4OCH_3$), 20.7 (2C), 20.6 (2C), 20.4 (2C), 20.2 (2C) (8×CO*C*H$_3$). HRMS Calcd for $C_{40}H_{50}O_{25}Na$ (M+Na): 953.2539; found 953.2541.

4.1.9. *p*-Methoxyphenyl β-D-galactopyranosyl-(1→3)-2-*O*-(β-D-galactopyranosyl)-α-L-arabinopyranosiduronic acid (1). To a solution of compound **13** (550 mg, mmol) in MeOH (10 mL) was added NaOMe (0.5 M in MeOH, 1 mL) and the solution was allowed to stir at room temperature for 6 h. Then the solution was neutralized with DOWEX 50W H^+ and filtered. The filtrate was evaporated to afford pure compound **1** (305 mg, 87%) as amorphous white solid. $[\alpha]_D^{25}$ +72 (*c* 1.0, H_2O). IR (KBr): 2373, 1758, 1608, 1389, 1229, 1049, 741 cm^{-1}; ^{1}H NMR (300 MHz, D_2O) δ: 6.91 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.79 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 4.99 (d, 1H, *J* 6.9 Hz, H-1), 4.57 (d, 1H, *J* 7.8 Hz, H-1′), 4.54 (d, 1H, *J* 7.8 Hz, H-1″), 3.62 (s, 3H, $C_6H_5CH_3$). ^{13}C NMR (75 MHz, D_2O) δ: 170.8 (*C*OOH), 153.3, 148.9, 116.4 (2C), 113.7 (2C) (ArC), 102.1 (C-1′), 102.0 (C-1″), 98.5 (C-1), 79.2, 76.2, 73.6, 72.7, 71.2, 70.9, 70.2, 69.1, 68.3, 67.0, 66.1, 63.7, 58.8, 54.5 ($C_6H_4OCH_3$). HRMS Calcd for $C_{24}H_{34}O_{17}Na$ (M+Na): 617.1694; found 617.1696.

4.1.10. *p*-Methoxyphenyl 4-*O*-acetyl-α-L-arabinopyranoside (14). To a slurry of compound **3** (2 g, 7.8 mmol) in dry CH_3CN (25 mL) was added trimethyl orthoacetate (1.5 mL, 11.7 mmol) followed by CSA (20 mg) and the slurry was allowed to stir at room temperature for 1 h when the starting material was converted completely to a faster moving component (R_f 0.7, *n*-hexane–EtOAc; 1:1). The solution was neutralized with Et_3N and the solvents were evaporated. The residue was dissolved in 80% aq AcOH (30 mL) and the solution was allowed to stir at room temperature for 45 min. After evaporating the solvents in vacuo and co-evaporating with toluene, the residue was purified by flash chromatography using 1:1–2:1 EtOAc–*n*-hexane to afford pure compound **14** (2 g, 86%) as white foam. $[\alpha]_D^{25}$ +49 (*c* 1.1, MeOH). IR (KBr): 2953, 2377, 1701, 1593, 1271, 1089, 1017, 719 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ: 7.02 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$),

6.80 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.13 (br s, 1H, O*H*), 4.93 (m, 1H, H-4), 4.76 (d, 1H, *J* 6.8 Hz, H-1), 4.60 (br s, 1H, O*H*), 3.94 (d, 1H, *J* 13.2 Hz, H-5a), 3.85–3.78 (m, 2H, H-2, H-3), 3.76 (s, 3H, $C_6H_4OCH_3$), 3.64 (d, 1H, *J* 13.2 Hz, H-5b), 2.14 (s, 3H, $COCH_3$). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ: 170.4 ($COCH_3$), 154.7, 150.7, 118.9 (2C), 114.0 (2C) (ArC), 102.1 (C-1), 70.9, 70.7, 70.0, 63.4 (C-5), 55.1 ($C_6H_4OCH_3$), 20.4 ($COCH_3$). HRMS Calcd for $C_{14}H_{22}O_7N$ (M+NH_4): 316.1396; found 316.1395.

4.1.11. *p*-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→3)-4-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-arabinopyranoside (15). A mixture of compound **14** (1.0 g, 3.4 mmol), compound **5** (3.8 g, 8.4 mmol), and MS 4 Å (3 g) in dry CH_2Cl_2 (40 mL) was stirred under nitrogen for 1 h. NIS (2.5 mg, 10.9 mmol) was added and the mixture was cooled to 10 °C followed by addition of H_2SO_4–silica (30 mg), and the mixture was allowed to stir at the same temperature for 1 h when all acceptor **14** was consumed (TLC). The mixture was immediately filtered through a pad of Celite and the filtrate was washed successively with $Na_2S_2O_3$ (2×30 mL), $NaHCO_3$ (2×30 mL), and brine (30 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated. The crude product thus obtained was purified by flash chromatography using *n*-hexane–EtOAc (1:1–1:2) to get the pure trisaccharide **15** (2.7 g, 84%) as white foam. $[\alpha]_D^{25}$ +99 (*c* 1.0, $CHCl_3$). IR (KBr): 2944, 2372, 1771, 1587, 1386, 1253, 1051 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 6.97 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.83 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 5.39 (br d, 2H, *J* 3.0 Hz, H-4′, H-4″), 5.30 (br d, 1H, *J* 3.0 Hz, H-4), 5.27 (m, 2H, H-1, H-3′), 5.08 (t, 1H, *J* 10.2 Hz, H-2′), 5.07 (t, 1H, *J* 10.2 Hz, H-2″), 5.00 (dd, 1H, *J* 3.0, 10.2 Hz, H-3″), 4.78 (d, 1H, *J* 8.1 Hz, H-1′), 4.67 (d, 1H, *J* 8.1 Hz, H-1″), 4.22–3.85 (m, 9H, H-2, H-3, H-5a, H-5′, H-5″, H-6a′, H-6a″, H-6b′, H-6b″), 3.76 (s, 3H, $C_6H_4OCH_3$), 3.49 (dd, 1H, *J* 3.3, 11.4 Hz, H-5b), 2.17, 2.15, 2.09, 2.07, 2.05, 2.00, 1.98, 1.97, 1.93 (9s, 27H, 9×$COCH_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.2 (2C), 170.0 (2C), 169.8 (3C), 169.7, 169.6 (2C), 169.1 (9×$COCH_3$), 155.1, 149.7, 118.0 (2C), 114.5 (2C) (ArC), 100.7 (C-1′ or C-1″), 100.6 (C-1′ or C-1″), 98.1 (C-1), 76.1, 74.6, 70.9, 70.7 (2C), 68.9, 68.7 (2C), 67.0, 66.7 (2C), 61.2, 60.8, 55.5 ($C_6H_4OCH_3$), 20.8 (2C), 20.7 (3C), 20.6 (2C), 20.5 (2C) (9×$COCH_3$). HRMS Calcd for $C_{42}H_{58}O_{25}N$ (M+NH_4): 976.3298; found 976.3300.

4.1.12. *p*-Methoxyphenyl β-D-galactopyranosyl-(1→3)-2-*O*-(β-D-galactopyranosyl)-α-L-arabinopyranoside (2). To a solution of compound **15** (1 g, 1.0 mmol) in MeOH (20 mL) was added NaOMe (0.5 M in MeOH, 2 mL) and the solution was stirred at room temperature for 6 h. After neutralizing the solution with DOWEX 50W H^+, the mixture was filtered and the filtrate was evaporated in vacuo to afford pure compound **2** (540 mg, 89%) as white powder. $[\alpha]_D^{25}$ +38 (*c* 0.8, H_2O). IR (KBr): 2367, 1693, 1203, 778 cm^{-1}; ^1H NMR (300 MHz, D_2O) δ: 6.95 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 6.83 (d, 2H, *J* 9.0 Hz, $C_6H_4OCH_3$), 4.97 (d, 1H, *J* 7.2 Hz, H-1), 4.61 (d, 1H, *J* 7.8 Hz, H-1′), 4.57 (d, 1H, *J* 7.8 Hz, H-1″), 3.69 (s, 3H, $C_6H_5CH_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 154.4, 150.8, 117.9 (2C), 114.5 (2C) (ArC), 104.1 (C-1′ or C-1″), 103.9 (C-1′ or C-1″), 100.0 (C-1), 79.1, 76.9, 75.5, 74.9, 73.4 (2C), 70.9, 70.4, 68.3, 67.9, 64.4, 60.6 (2C), 59.9, 55.4 ($C_6H_4OCH_3$). HRMS Calcd for $C_{24}H_{36}O_{16}Na$ (M+Na): 603.1901; found 603.1903.

Acknowledgements

S.D. is thankful to CSIR, New Delhi for providing fellowship. Instrumentation facilities from SAIF, CDRI are gratefully acknowledged. The work is funded by Department of Science and Technology, New Delhi, India by SERC Fast-Track Grant SR/FTP/CS-110/2005.

References and notes

1. Yeung, B. K. S.; Hamann, M. T.; Scheuer, P. J.; Kellyborges, M. *Tetrahedron* **1994**, *50*, 12593–12598.
2. Ryu, G.; Choi, B. W.; Lee, B. H.; Hwang, K. H.; Lee, U. C.; Jeong, D. S.; Lee, N. H. *Tetrahedron* **1999**, *55*, 13171–13178.
3. Dai, H. F.; Edrada, R. A.; Ebel, R.; Nimtz, M.; Wray, V.; Proksch, P. *J. Nat. Prod.* **2005**, *68*, 1231–1237.
4. Sandler, J. S.; Forsburg, S. L.; Faulkner, D. J. *Tetrahedron* **2005**, *61*, 1199–1206 and references therein.
5. Antonov, A. S.; Afiyatullov, S. S.; Kalinovsky, A. I.; Ponomarenko, L. P.; Dmitrenok, P. S.; Aminin, D. L.; Agafonova, I. G.; Stonik, V. A. *J. Nat. Prod.* **2003**, *66*, 1082–1088.
6. Campagnuolo, C.; Fattorusso, E.; Taglialatela-Scafati, O. *Tetrahedron* **2001**, *57*, 4049–4055.
7. Okada, Y.; Matsunaga, S.; van Soest, R. W. M.; Fusetani, N. *J. Org. Chem.* **2006**, *71*, 4884–4888.
8. Chauvin, A.-L.; Nepogodiev, S. A.; Field, R. A. *J. Org. Chem.* **2005**, *70*, 960–966.
9. Lipták, A.; Imre, J.; Nánási, P. *Carbohydr. Res.* **1981**, *92*, 154–156.
10. For the use of H_2SO_4–silica in carbohydrate synthesis see: (a) Mukhopadhyay, B. *Tetrahedron Lett.* **2006**, *47*, 4337–4341; (b) Rajput, V. K.; Mukhopadhyay, B. *Tetrahedron Lett.* **2006**, *47*, 5939–5941; (c) Rajput, V. K.; Roy, B.; Mukhopadhyay, B. *Tetrahedron Lett.* **2006**, *47*, 6987–6991; (d) Dasgupta, S.; Roy, B.; Mukhopadhyay, B. *Carbohydr. Res.* **2006**, *341*, 2708–2713; (e) Roy, B.; Mukhopadhyay, B. *Tetrahedron Lett.* **2007**, *48*, 3783–3787; For the use of H_2SO_4–silica in organic synthesis, see: (f) Zolfigol, M. A.; Bamoniri, A. *Synlett* **2002**, 1621–1623; (g) Zolfigol, M. A. *Tetrahedron* **2001**, *57*, 9509–9511; (h) Zolfigol, M. A.; Shirini, F.; Ghorbani Choghamarani, A.; Mohammadpoor-Baltork, I. *Green Chem.* **2002**, *4*, 562–564; (i) Shirini, F.; Zolfigol, M. A.; Mohammadi, K. *Bull. Korean Chem. Soc.* **2004**, *25*, 325–327; For similar type of glycosylations using $HClO_4$–silica, see: (j) Mukhopadhyay, B.; Maurer, S. V.; Rudolph, N.; van Well, R.; Russell, D. A.; Field, R. A. *J. Org. Chem.* **2005**, *70*, 9059–9062; (k) Mukhopadhya, B.; Collet, B.; Field, R. A. *Tetrahedron Lett.* **2005**, *46*, 5923–5925; (l) Mukhopadhyay, B.; Field, R. A. *Carbohydr. Res.* **2006**, *341*, 1697–1701; (m) Du, Y.; Wei, G.; Cheng, S.; Hua, Y.; Linhardt, R. J. *Tetrahedron Lett.* **2006**, *47*, 307–310.
11. Gent, P. A.; Gigg, R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1446–1455.
12. Limberg, G.; Thiem, J. *Carbohydr. Res.* **1995**, *275*, 107–115.

13. Kinzy, W.; Schmidt, R. R. *Liebigs Ann. Chem.* **1985**, 1537–1545.
14. Huang, L.; Teumelsan, N.; Huang, X. *Chem.—Eur. J.* **2006**, *12*, 5246–5252.
15. (a) Davis, N. J.; Flitsch, S. L. *Tetrahedron Lett.* **1993**, *34*, 1181–1184; (b) de Nooy, A. E. J.; Besemer, A. C.; van Bekkum, H. *Synthesis* **1996**, 1153–1174; (c) Baisch, G.; Ohrlein, R. *Carbohydr. Res.* **1998**, *312*, 61–72; (d) Li, K. C.; Helm, R. F. *Carbohydr. Res.* **1995**, *273*, 249–253.
16. Perrin, D. D.; Amarego, W. L.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon: London, 1996.