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Carbohydrate Research 343 (2008) 957–964
Carbohydrate RESEARCH

Note

Versatile acetylation of carbohydrate substrates with bench-top sulfonic acids and application to one-pot syntheses of peracetylated thioglycosides

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Received 20 November 2007; received in revised form 9 January 2008; accepted 16 January 2008
Available online 26 January 2008

Abstract—Inexpensive and readily available sulfonic acids, *p*-toluenesulfonic acid, and sulfuric acid are versatile and efficient catalysts for the peracetylation of a broad spectrum of carbohydrate substrates in good yield and in a practical time frame. Three appealing features in sulfonic acid-catalyzed acetylation of free sugars were explored including (1) suppression of furanosyl acetate formation for D-galactose and L-fucose; (2) high yielding chemoselective acetylation of sialic acid under appropriate conditions; and (3) peracetylation of amino sugars with different amino protecting functions. Simple one-pot two step acetylation–thioglycosidation methods for the expeditious synthesis of *p*-tolyl per-*O*-acetyl thioglycosides were also delineated.

Keywords: *p*-Toluenesulfonic acid; Acid-catalyzed acetylation; Amino sugars; One-pot protecting group manipulation

Chemical synthesis of oligosaccharides is a two-stage process that comprises the preparation of glycosyl building blocks followed by their assemblage.[1] Different synthetic strategies have emerged to speed up the assembling process, which include the armed-disarmed approach,[2] orthogonal glycosylation,[3] reactivity-based one-pot glycosylation,[4] sequential iterative glycosylation,[5] and automated solid phase oligosaccharide synthesis.[6] The implementation of these strategies relies heavily on the facile synthesis of glycosyl building blocks. Thioglycoside derivatives constitute a major class of glycosyl building blocks for oligosaccharide synthesis,[7] which are mainly derived from per-*O*-acetyl thioglycosides.

Conventional preparation of per-*O*-acetyl thioglycosides involves peracetylation and subsequent thioglycosidation.[8] However, classical carbohydrate acetylation uses excess pyridine; not only is pyridine highly toxic, but the presence of excess basic reagent makes the one-pot operation impossible.[9] Provided that the first peracetylation is an acid-catalyzed process, which is compatible to the second thioglycosidation; a one-pot acetylation–thioglycosidation is foreseeable. Thus, various one-pot strategies for the preparation of per-*O*-acetyl thioglycosides have been developed, although most of the existing methods have pitfalls originating from the peracetylation process.[10] For example, the formation of undesired furanosyl acetates for some sugars in acid-catalyzed acetylation compromises the yield in the subsequent thioglycosidation.[10c,e,11] The strong Lewis acid character of some acids makes them less suitable for the peracetylation of N-protected amino sugars and thus limits the scope of application to carbohydrate substrates without amino functions.[10d,e,12–14] Herein, we report a versatile and high yielding (75–95%) carbohydrate peracetylation protocol that can overcome the above drawbacks by using common sulfonic acids in the appropriate reaction conditions. Subsequent development of the simple one-pot two step acetylation–thioglycosidation protocols for the expeditious syntheses of *p*-tolyl per-*O*-acetyl thioglycosides was also delineated.

p-Toluenesulfonic acid monohydrate (TsOH)[15] and sulfuric acid (H_2SO_4)[16,17] are known catalysts for

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0008-6215/$ - see front matter
doi:10.1016/j.carres.2008.01.014

hydroxyl acetylation in the presence of excess acetic anhydride, however their efficiency with near stoichiometric acetic anhydride has not been explored. In addition, TsOH has never been used for the acetylation of free sugar substrates. Although silica-supported H_2SO_4 and $HClO_4$ have been used for carbohydrate acetylation, the additional immobilization step makes these protocols less convenient and the use of potentially explosive $HClO_4$ is also discouraged.[14a,b] Our initial observations showed that both neat H_2SO_4 and TsOH exhibited sufficient catalytic efficiency (1 mol % per OH group of the sugar) for the acetylation of D-glucose with a near stoichiometric amount of Ac_2O. Peracetylation of D-glucose with H_2SO_4 was completed in 0.2 h while with TsOH the reaction needed 8 h; such a difference should be useful for the selective peracetylation of sugars under different reaction conditions.

In the standard protocol, TsOH (1 or 2 mol % per OH group of the sugar) in Ac_2O (Table 1, entries a–c, h, and m) or in a mixture of Ac_2O and acetonitrile (CH_3CN) (Table 1, entries d–g, i–l, and n–o) was added to the carbohydrate substrate with stirring at 0 °C for 1 h. Subsequently, the reaction mixture was warmed to the optimal reaction temperature; detailed experimental conditions are given in Table S1 of Supplementary data. In general, a near stoichiometric amount of Ac_2O (1.2 mol equiv per OH group of the sugar) was employed. For carbohydrate substrates without amino functions, the desired peracetylated glycosyl acetates were furnished in good to excellent (75–95%) yield (Table 1, entries a, b, c, m, n, and o).

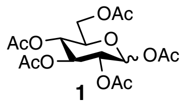
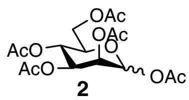
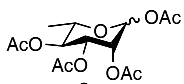
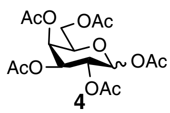
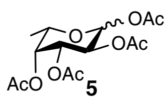
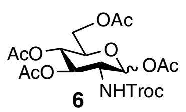
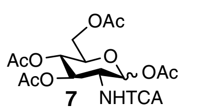
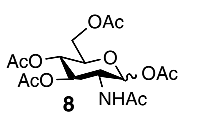
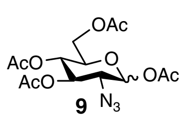
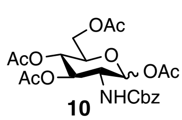
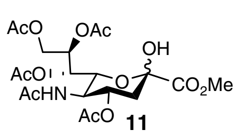
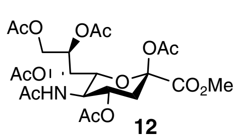
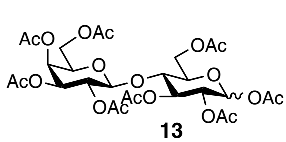
Acetylation of D-galactose and L-fucose requires special attention as both are prone to form undesired furanosyl acetates. Such furanosyl isomers were also formed from the sugars with our standard TsOH-catalyzed acetylation protocol (30% relative to total peracetyl acetates for D-galactose, 26% relative to total peracetyl acetates for L-fucose).[10c,e,11] Gratifyingly, the furanosyl isomer derived from D-galactose was gradually reduced by decreasing the reaction temperatures and nearly complete elimination was accomplished at 0 °C.[10e,15b] At such low reaction temperature, the more reactive H_2SO_4 was needed. However for the acetylation of L-fucose, 7% of furanosyl isomer was formed at 0 °C and thus further decrease in the temperature to −20 °C was required. Under the optimal reaction conditions, the formation of furanosyl isomer was reduced to less than 2% (see spectroscopic in Supplementary data page S23).

After examining the simple carbohydrate substrates, we turned to the amino sugars, which occur in the majority of natural oligosaccharides. Although pyridine-catalyzed acetylation works well for the acetylation of amino sugars, the less toxic TsOH-catalyzed protocol should provide a desirable alternative.[9] As different amino protecting functions have been used in oligosaccharide synthesis, it would be worthy knowing the compatibility of our protocol to such protecting functions. To this end, D-glucosamines with trichloroethoxycarbonyl (Troc), trichloroacetyl (TCA), acetyl (Ac), azido (N_3), and benzylethoxycarbonyl (Cbz) functions were prepared and acetylated with the standard TsOH-catalyzed protocol (Table 1, entries f–j).[18] To our delight, the desired peracetylated products **6–10** were furnished within 3–6 h in respectable 85–94% yield. For the acetylation of *N*-acetyl neuraminic acid methyl ester (NANA methyl ester), 4,7,8,9-tetra-*O*-acetyl NANA methyl ester **11** was obtained exclusively in 90% yield without any trace of the pentaacetylated product (Table 1, entry k). Such chemoselectivity is superior to the conventional $HClO_4$-catalyzed protocol.[19] To obtain the pentaacetyl product, a higher reaction temperature (45 °C) and excess Ac_2O were required, and 2,4,7,8,9-pentacetyl NANA methyl ester **12** was furnished in 80% yield along with 5% elimination product (Table 2, entry l). As **11** and **12** are valuable precursors for the synthesis of sialic acid-containing oligosaccharides, our new procedure should provide a more convenient alternative.

It should also be mentioned that the facile acetylation of amino sugars with the TsOH-catalyzed protocol was in sharp contrast to the reaction using I_2.[12] As a comparison, the amount of acid catalyst (in mol % per OH group), reaction time, and product yield for the acetylation of *N*-Troc glucosamine, *N*-acetyl glucosamine, and NANA methyl ester with I_2-catalyzed and TsOH-catalyzed protocols are provided in Table 1 (entries f, h, k and l). For the acetylation of *N*-Troc glucosamine with I_2, the reported experimental procedure was followed and 250 mg I_2 per g of *N*-Troc glucosamine (9 mol % per OH group) was used.[12] For the I_2-catalyzed acetylation of GlcNAc and NANA methyl ester, a much higher catalyst loading was applied (either 5 or 13 mol % per OH group for the I_2-catalyzed acetylation versus 2 mol % per OH group for the TsOH-catalyzed acetylation) (Table 1, entries, h, k, and l). Even at such a high I_2 concentration, it still took two days for the complete acetylation of *N*-acetyl glucosamine (Table 1, entry h). In addition, no significant acetylation was observed for *N*-Troc glucosamine when I_2 catalyst was used (Table 1, entry f).

Regarding the α-/β-selectivity of the process, α-glycosyl acetates were formed preferentially in majority of the cases, which can be explained by thermodynamics (Table 1, entries a–e, g–h, and m). Nevertheless, for the acetylation of *N*-Troc and 2-azido-2-deoxy-glucosamines, β-glycosyl acetates were the major anomers obtained (Table 1, entries f and i). Apparently, the strong participatory effect of trichloroethoxylcarbamyl function outweighed the anomeric effect in *N*-Troc glucosamine, while the reason for β-selectivity in 2-azido-2-dexoy-glucosoamine is not clear.

Table 1. Sulfonic acid-catalyzed acetylation for carbohydrate substrates with different complexities

Entry	Carbohydrate substrate	Per-*O*-acetyl glycosyl acetate	Acid (mol % per OH)	Temp (°C)	Time (h)	Yield % (α:β)
a	D-Glucose	 **1**	TsOH (2)	0–27	6	95 (71:29)
b	D-Mannose	 **2**	TsOH (2)	0–27	5	94 (45:11)
c	L-Rhamnose·H_2O	 **3**	TsOH (2)	0–27	4	92 (58:42)
d	D-Galactose	 **4**	H_2SO_4 (2)	−20 to 0	18	92 (76:24)[a]
e	L-Fucose	 **5**	H_2SO_4 (2)	−30 to −20	8	93 (9:1)[a]
f	2-Trichloroethoxy carbamyl-2-deoxy-D-glucopyranose	 **6**	TsOH (2) I_2 (9)	0–27 0–27	6 >24	90 (27:73)[a] No reaction[b]
g	2-Trichloroacetamido-2-deoxy-D-glucopyranose	 **7**	TsOH (2)	0–55	5	93 (77:23)[a]
h	2-Acetamido-2-deoxy-D-glucopyranose	 **8**	TsOH (2) I_2 (5)	0–50 0–27	5 48	90 (61:39) 98 (2.5:1)[b,c]
i	2-Azido-2-deoxy-D-glucopyranose	 **9**	TsOH (2)	0–27	4	85 (23:77)[a]
j	2-Benzyloxycarbamyl-2-deoxy-D-glucopyranose	 **10**	TsOH (2)	0–40	3	94 (not determined)[a]
k	*N*-Acetyl neuraminic acid methyl ester	 **11**	TsOH (2) I_2 (6.5) I_2 (13)	0–27 0–27 0–27	4 Sluggish 20 min	90 (1:4)[a] Not determined[b,c] 70 (not determined)[b,c]
l	*N*-Acetyl neuraminic acid methyl ester	 **12**	TsOH (2) I_2 (13)	0–45 0–35	12 60 min	80 (β only)[a,b] 90 (1:3.5)[b,c]
m	D-Lactose·H_2O	 **13**	TsOH (2)	0–40	4	90 (3:2)

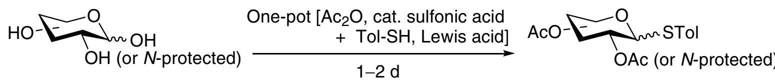
(*continued on next page*)

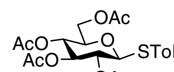
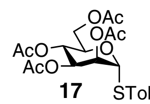
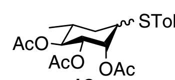
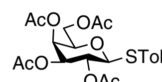
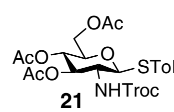
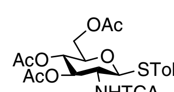
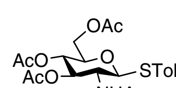
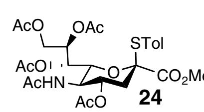
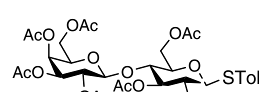
Table 1 (*continued*)

Entry	Carbohydrate substrate	Per-*O*-acetyl glycosyl acetate	Acid (mol % per OH)	Temp (°C)	Time (h)	Yield % (α:β)
n	β-Cylcodextrin	per-*O*-acetyl-β-cylcodextrin **14**	TsOH (1)	0–40	10	90[a]
o	D(+)-Melezitose·H_2O	per-*O*-acetyl-D(+)-Melezitose **15**	TsOH (1)	0–30	6	75[a]

[a] CH_3CN was added to the reaction mixture.
[b] Excess Ac_2O was used.
[c] Ref. 12.

Table 2. One-pot syntheses of per-*O*-acetyl thioglycosides



Entry	Carbohydrate substrate	Thioglycoside	Yield % (α:β)
a	D-Glucose	 **16**	75 (β only)[a]
b	D-Mannose	 **17**	80 (α only)[a]
c	L-Rhamnose·H_2O	 **18**	84 (5:1)[a]
d	D-Galactose	 **19**	68 (β only)[a]
e	L-Fucose	 **20**	75 (β only)[a]
f	2-Trichloroethoxy carbamyl-2-deoxy-D-glucopyranose	 **21**	72 (β only)[a]
g	2-Trichloroacetamido-deoxy-D-glucopyranose	 **22**	65 (β only)[a]
h	2-Acetamido-2-deoxy-D-glucopyranose	 **23**	65 (β only)[b]
i	*N*-Acetyl neuraminic acid methyl ester	 **24**	72 (β only)[a]
k	D-Lactose·H_2O	 **25**	75 (β only)[a]

[a] $BF_3 \cdot Et_2O$ was used for thioglycosidation.
[b] $SnCl_4$ was used for thioglycosidation.

With the sulfonic acid-catalyzed acetylation protocols in hand, we next explored a simple one-pot two step acetylation–thioglycosidation approach for the preparation of per-*O*-acetyl thioglycosides. In the one-pot TsOH-catalyzed acetylation–thioglycosidation, the sugar substrate was firstly peracetylated with the described TsOH-catalyzed acetylation, followed by the solvent removal, and the addition of *p*-thiocresol (1.5 mol equiv) in dichloromethane (CH_2Cl_2) and the appropriate Lewis acid catalyst ($BF_3{\cdot}Et_2O$ or $SnCl_4$) (Table 2, entries a–c and f–k). The optimal reaction conditions and exact amount of reagents used are detailed in Table S2 of Supplementary data. In the one-pot H_2SO_4-catalyzed acetylation–thioglycosidation of D-galactose and L-fucose, complete removal of solvent led to undesired dehydration; thus 1.2 equiv of methanol was added to quench the remaining Ac_2O, followed by the addition of thiocresol (2 mol equiv) in CH_2Cl_2 and $BF_3{\cdot}Et_2O$ (2 mol equiv). Simple hexopyranoses (Table 2, entries a–e), glucosamines with different amino protecting functions (Table 2, entries f–h), NANA methyl ester (Table 2, entry i), and lactose (Table 2, entry k) were smoothly converted to the expected per-*O*-acetyl thioglycosides **15**–**25** in respectable yields (65–84%) within 1–2 days. Both *N*-Cbz and N_3 protecting functions were dismantled under these thioglycosidation conditions. Due to the participation of the group at C2, the 1,2-*trans* thioglycosidic bond was formed exclusively in most cases, whereas for L-rhamnose, a 5:1 α- to β-thioglycosides mixture was furnished, which also agreed with previous finding (Table 2, entry c).[10e] For NANA methyl ester, the β-thioglycoside **24** was formed exclusively, which could be attributed to the anomeric effect (Table 2, entry i).

In conclusion, cheap and readily available sulfonic acids, TsOH, and H_2SO_4 are versatile and efficient catalysts for the acetylation of carbohydrates. Contrary to most acid catalysts, which are mainly restricted to the acetylation of simple carbohydrates without amino functions,[10d,e,12–14] our versatile protocol can be applied to different carbohydrate substrates including mono-, di-, tri-, and hepta-saccharides, amino sugars with different amino protecting functions, and oligosaccharides containing fragile furanosyl glycosidic bonds. Additional features include the chemoselective formation of tetra-*O*-acetyl- and penta-*O*-acetyl-NANA esters. In addition, the simple one-pot two step acetylation–thioglycosidation protocols were also developed for the direct access of a panel of *p*-tolyl per-*O*-acetyl thioglycosides including the first one-pot preparation of a sialyl thioglycoside.

1. Experimental

1.1. General methods

All chemicals were purchased as reagent grade and used without further purification. TsOH was dried over P_2O_5 under vacuum and stored in desiccators. 99.99% H_2SO_4 used was purchased from a known chemical vendor. CH_3CN and CH_2Cl_2 were distilled over calcium hydride under N_2 before use. Flash column chromatography was performed on silica gel 60 (70–230 mesh, E. Merck). ^1H and ^{13}C NMR spectra of the prepared compounds were recorded with 300 MHz and 75 MHz Bruker spectrometers. Chemical shift (δ ppm) was measured against TMS, generated from the residual $CHCl_3$ lock signal at δ 7.26 ppm against the residual proton signal of deuterated chloroform, and the ^{13}C resonance signal is calibrated against the ^{13}C signal of deuterated chloroform. Coupling constant(s) in Hertz (Hz) were obtained from ^1H NMR spectra.

1.2. TsOH-catalyzed acetylation procedure for the preparation of per-*O*-acetyl glycosyl acetates 1–3 and 6–15

To 0.5 g of mono-, di-, tri-, or hepta-saccharides was added Ac_2O (or a mixture of Ac_2O and CH_3CN) in which a catalytic amount of TsOH was dissolved. The mixture was firstly stirred at 0 °C for 1 h and then stirred at the optimal reaction temperature.[19] Upon complete acetylation, the mixture was diluted with EtOAc (20 mL), which was washed with cold satd $NaHCO_3$ (20 mL × 2), water (20 mL × 1), brine (20 mL × 1), dried over $MgSO_4$, filtered, and then concentrated. Except for melezitose and N-protected amino sugars, the crude concentrate after work-up was directly characterized with NMR spectroscopy. For the peracetylated products of melezitose and N-protected amino sugars, flash chromatography purification with EtOAc–hexane elution was performed.

1.3. H_2SO_4-catalyzed acetylation procedure for the preparation of per-*O*-acetyl glycosyl acetates 4 and 5

To a suspension of 0.5 g of D-galactose in a mixture of Ac_2O–CH_3CN at −20 °C (or −30 °C for L-fucose) was added catalytic amount of H_2SO_4 in CH_3CN (neat H_2SO_4 was diluted with CH_3CN to a 10% v/v solution). The exact amount of reagents used and specific reaction conditions were detailed in Supplementary data.[19] After stirring for 1 h at −20 °C (or −30 °C for L-fucose), the temperature was gradually warmed up to 0 °C (−20 °C for L-fucose) and the stirring was continued till the end of the reaction. The workup procedure was processed as described above.

1.4. One-pot TsOH-catalyzed acetylation–thioglycosidation procedure for the preparation of per-*O*-acetyl thioglycosides of 16–18 and 21–25

The peracetylation procedure was performed at 0.5 g sugar substrate scale as described above. Upon complete acetylation, the reaction solvent was removed and co-evaporated twice with an equal volume of toluene on a rotary evaporator. Thiocresol (1.5 mol equiv) in CH_2Cl_2 was added to the crude residue at 0 °C, followed by the addition of Lewis acid (either 2 mol equiv of $BF_3 \cdot Et_2O$ or 1.1 mol equiv of $SnCl_4$), and the mixture was stirred initially at 0 °C under N_2. After the addition of the reagents, the reaction temperature was raised to 27 °C and the reaction mixture stirred until the end of the reaction, except for *N*-acetyl-D-glucosamine **8**, in which the reaction mixture was warmed up to 40 °C. Upon completion of the reaction, the mixture was diluted with cold EtOAc (50 mL), which was sequentially washed with cold satd $NaHCO_3$ (30 mL × 2), brine (30 mL × 1), dried over $MgSO_4$, filtered, and then concentrated for flash column chromatography to furnish the per-*O*-acetyl thioglycosides **16–18** and **21–25**.

1.5. One-pot H_2SO_4-catalyzed acetylation–thioglycosidation procedure for the preparation of per-*O*-acetyl thioglycosides 19 and 20

The peracetylation procedure of D-galactose or L-fucose was performed at 0.5 g scale as described above. Upon complete acetylation, 1.2 equiv of methanol was added and the mixture was stirred for 1 h at 0 °C; subsequent addition of thiocresol (1.5 mol equiv) in CH_2Cl_2 and $BF_3 \cdot Et_2O$ followed. The mixture was stirred initially at 0 °C and then gradually warmed to room temperature (27 °C) under N_2. Upon completion of the reaction, the mixture was diluted with cold EtOAc (50 mL), which was washed with cold satd $NaHCO_3$ (30 mL × 2), brine (30 mL × 1), dried over $MgSO_4$, filtered, and then concentrated for flash column chromatography to furnish the per-*O*-acetyl thioglycosides **19** and **20**.

1.6. *p*-Tolyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (16)

^1H NMR (300 MHz, $CDCl_3$) δ: 7.39 (d, $J = 8.1$ Hz, 2H, ArH), 7.10 (d, $J = 7.9$ Hz, 2H, ArH), 5.20 (dd, $J = 9.3$, 9.4 Hz, 1H, H-3), 5.01 (dd, $J = 9.3$, 9.9 Hz, 1H, H-4), 4.92 (dd, $J = 9.3$, 10.0 Hz, 1H, H-2), 4.63 (d, $J = 9.9$ Hz, 1H, H-1), 4.20–4.14 (m, 2H, H-6, H-6), 3.70 (ddd, $J = 2.6$, 4.7, 10.1 Hz, 1H, H-5), 2.33 (s, 3H, STol CH_3), 2.09 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.01 (s, 3H, Ac), 1.98 (s, 3H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.97, 170.58, 169.78, 169.63, 139.2, 134.2, 130.2, 130.1, 127.9, 86.2, 76.1, 70.3, 68.6, 62.5, 21.58, 21.16, 21.12, 20.97.

1.7. *p*-Tolyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranoside (17)

^1H NMR (300 MHz, $CDCl_3$) δ: 7.40 (d, $J = 8.1$ Hz, 2H, ArH), 7.12 (d, $J = 8.1$ Hz, 2H, ArH), 5.50 (dd, $J = 1.5$, 2.5 Hz, 1H), 5.42 (d, $J = 1.0$ Hz, 1H, H-1), 5.34–5.32 (m, 2H), 4.57–4.56 (m, 1H), 4.30 (dd, $J = 12.3$, 6.0 Hz, 1H), 4.10 (dd, $J = 12.5$, 2.6 Hz, 1H), 2.34 (s, 3H, STol CH_3), 2.15 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.08 (s, 3H, Ac), 1.99 (s, 3H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.0, 170.3, 170.22, 170.16, 138.8, 122.0, 130.4, 129.2, 86.4, 69.8, 69.7, 66.8, 62.9, 21.52, 21.27, 21.09, 21.03.

1.8. *p*-Tolyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (18)

^1H NMR (300 MHz, $CDCl_3$) δ: 7.36 (d, $J = 8.1$ Hz, 2H, ArH), 7.11 (d, $J = 8.1$ Hz, 2H, ArH), 5.48 (dd, $J = 3.3$, 1.5 Hz, 1H, H-2), 5.32 (d, $J = 1.5$ Hz, 1H, H-1), 5.27 (dd, $J = 3.3$, 9.9 Hz, 1H, H-2), 5.13 (t, $J = 9.9$ Hz, 1H, H-4), 4.41–4.32 (m, H-5), 2.32 (s, 3H, STol CH_3), 2.14 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.00 (s, 3H, Ac), 1.24 (s, 3H, CH_3-R); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.4, 170.3, 138.6, 132.8, 130.4, 130.3, 129.7, 86.4, 71.6 × 2, 69.7, 68.1, 21.52, 21.30, 21.21, 21.08, 17.7.

1.9. *p*-Tolyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (19)

^1H NMR (300 MHz, $CDCl_3$) δ: 7.39 (d, $J = 8.1$ Hz, 2H, ArH), 7.10 (d, $J = 7.8$ Hz, 2H, ArH), 5.4 (dd, $J = 1.0$, 3.3 Hz, 1H, H-4), 5.22 (t, $J = 9.9$ Hz, 1H, H-2), 5.03 (dd, $J = 3.3$, 10.0 Hz, H-3), 4.64 (d, $J = 10.0$ Hz, H-1), 4.19 (dd, $J = 7.0$, 11.3 Hz, 1H, H-6), 4.11 (dd, $J = 6.3$, 11.3 Hz, H-6), 3.92 (dt, $J = 1.0$, 6.1 Hz, H-5), 2.34 (s, 3H, STol CH_3), 2.12 (s, 3H, Ac), 2.10 (s, 3H, Ac), 2.04 (s, 3H, Ac), 1.97 (s, 3H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.8, 170.62, 170.48, 169.84, 138.8, 133.5, 130.0, 129.0, 87.3, 72.4, 67.7, 67.6, 61.9, 21.56, 21.27, 21.07, 21.04, 20.99.

1.10. *p*-Tolyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside (20)

^1H NMR (300 MHz, $CDCl_3$) δ: 7.42 (d, $J = 8.1$ Hz, 2H, ArH), 7.13 (d, $J = 7.9$ Hz, 2H, ArH), 5.25 (dd, $J = 0.7$, 3.2 Hz, 1H, H-4), 5.19 (t, $J = 9.9$ Hz, 1H, 1H, H-2), 5.03 (dd, $J = 3.3$, 9.9 Hz, 1H, H-3), 4.64 (d, $J = 9.8$ Hz, 1H, H-1), 3.80 (q, $J = 6.4$ Hz, 1H, H-5), 2.33 (s, 3H, STol CH_3), 2.14 (s, 3H, Ac), 2.10 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.24 (d, $J = 6.4$ Hz, 3H, CH_3-R); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.1, 170.6, 169.9, 138.6, 133.3, 130.3, 130.0, 129.5, 8.2, 72.8, 70.7, 67.8, 21.6, 21.3, 21.09, 21.06, 16.8.

1.11. *p*-Tolyl 3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-2-trichloroethoxycarbamyl-β-D-glucopyranoside (21)

^1H NMR (300 MHz, $CDCl_3$) δ: 7.42 (d, $J = 8.1$ Hz, 2H, ArH), 7.13 (d, $J = 7.8$ Hz, 2H, ArH), 5.29–5.26 (m, 2H), 5.03 (t, $J = 9.8$ Hz, 1H, H-4), 4.79 (d, $J = 10.8$ Hz, 1H), 4.75 (d, $J = 10.9$ Hz, 1H), 4.23–4.17 (m, 2H), 3.74–3.65 (m, 2H), 2.36 (s, 3H, STol CH_3), 2.10 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.01 (s, 3H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.4, 171.0, 170.5, 169.8, 154.7, 139.0, 138.7, 134.1, 133.2, 130.3, 130.2, 95.8, 86.7, 75.1, 71.4, 63.8, 63.5, 55.7, 52.6, 21.5, 21.1, 21.07, 20.95.

1.12. *p*-Tolyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-1-thio-β-D-glucopyranoside (22)

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50 (br m, 1H, N–H), 7.39 (d, $J = 8.1$ Hz, 2H, ArH), 7.10 (d, $J = 7.9$ Hz, 2H, ArH), 5.41 (dd, $J = 9.3$, 11 Hz, 1H, H-3), 5.03 (t, $J = 9.6$ Hz, 1H, H-4), 4.75 (d, $J = 9.8$ Hz, 1H, H-1), 4.23–4.01 (m, 3H, H-6, H-2), 3.76 (ddd, $J = 2.5$, 4.6, 10.0 Hz, 1H, H-5), 2.32 (s, 3H, STol CH_3), 2.06 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.78 (s, 3H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.8, 171.0, 170.0, 162.2, 139.4, 134.5, 130.1, 128.2, 92.8, 87.2, 76.2, 73.9, 68.9, 62.8, 54.5, 21.6, 21.1, 21.0, 20.6.

1.13. *p*-Tolyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (23)

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.39 (d, $J = 8.1$ Hz, 2H, ArH), 7.10 (d, $J = 7.9$ Hz, 2H, ArH), 5.92 (br d, $J = 12$ Hz, 1H, N–H), 5.23 (dd, $J = 9.3$, 10.9 Hz, 1H, H-3), 5.03 (dd, $J = 9.3$, 9.9 Hz, 1H, H-4), 4.79 (d, $J = 9.9$ Hz, 1H, H-1), 4.20–4.17 (m, 2H, H-6, H-6′), 4.00 (dd, $J = 9.3$, 10.0 Hz, 1H, H-2), 3.71 (ddd, $J = 2.6$, 4.7, 10.1 Hz, 1H, H-5), 2.34 (s, 3H, STol CH_3), 2.09 (s, 3H, Ac), 2.01 (s, 3H, Ac), 1.99 (s, 3H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.4, 171.0, 170.5, 169.8, 162.4, 139.4, 134.5, 130.1, 128.2, 87.2, 76.2, 73.9, 68.9, 62.8, 54.5, 21.5, 21.1, 21.07, 20.95.

1.14. *p*-Tolyl 2-thio-β-D-*N*-acetyl-neuraminic acid methyl ester (24)

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.33 (d, $J = 12.8$ Hz, 2H, ArH), 7.12 (d, $J = 7.9$ Hz, 2H, ArH), 5.92 (br d, 1H, N–H), 5.48 (s, 1H), 5.39 (td, $J = 1.1$, 4.2 Hz, H-4), 4.96 (d, $J = 13.9$ Hz, 1H), 4.64 (dd, $J = 2.3$, 10.5 Hz, 1H), 4.50 (dd, $J = 1.9$, 12.2 Hz, 1H), 4.13 (dd, $J = 4.3$, 13.4 Hz, 1H), 4.03 (dd, $J = 8.7$, 7.2 Hz, 1H), 3.59 (s, 3H, CH_3O), 2.64 (dd, $J = 9.1$, 4.7 Hz, 1H), 2.32 (s, 3H, STol CH_3), 2.14 (s, 3H, Ac), 2.12 (s, 3H, Ac), 2.08 (s, 3H, Ac), 1.95 (s, 3H, Ac), 1.89 (s, 3H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 171.66, 171.40, 170.66, 170.63, 168.66, 140.5, 136.6, 130.2, 125.6, 89.3, 73.6, 73.5, 69.2, 69.1, 63.2, 52.9, 49.7, 37.8, 23.5, 21.69, 21.49, 21.30, 21.13, 21.09.

1.15. *p*-Tolyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-1-thio-β-D-glucopyranoside (25)

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.33 (d, $J = 8.2$ Hz, 2H, ArH), 7.07 (d, $J = 8.0$ Hz, 2H, ArH), 5.30 (dd, $J = 1.0$, 3.3 Hz, H-4′), 5.16 (t, $J = 9.9$ Hz, 1H), 5.05 (dd, $J = 9.3$, 9.4 Hz), 5.03 (dd, $J = 9.3$, 9.9 Hz, 1H), 4.93 (dd, $J = 3.3$, 10.0 Hz, 1H), 4.82 (dd, $J = 9.3$, 10.0 Hz, 1H), 4.57 (d, $J = 10.0$ Hz), 4.47–4.43 (m, 2H), 4.09–4.03 (m, 3H), 3.84 (t, $J = 6.3$ Hz, 1H), 3.70 (t, $J = 7.7$ Hz, 1H), 3.64 (m, 1H), 2.29 (s, 3H, STol CH_3), 2.13–1.92 (m, 21H, 7 × Ac); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.69, 170.64, 170.52, 170.42, 170.09, 169.92, 169.41, 138.9, 134.1, 132.8, 130.3, 130.0, 128.1, 101.3, 85.9, 77.0, 74.3, 71.3, 71.2, 71.1, 70.0, 66.9, 62.4, 61.2, 21.55, 21.22, 21.17, 21.01, 20.99, 20.88.

Acknowledgments

We thank Professor H.-F. Chow of Chinese University of Hong Kong for advice in manuscript preparation, Professor Y. C. Chen for performing MALDI TOF MS analysis of per-*O*-acetyl-β-D-cyclodextrin and we are indebted to Professor C.-Y. Wu of Academic Sinica in Taiwan for providing *N*-acetyl neuraminic acid as gift for the study. This work was supported by the National Science Council of Taiwan ROC (NSC 94-2119-M-009-002).

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2008.01.014.

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