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Note

Selective deprotection of terminal isopropylidene acetals and trityl ethers using $HClO_4$ supported on silica gel☆

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Abstract—Terminal isopropylidene acetals are selectively cleaved to the corresponding 1,2-diols in good to excellent yields in 6–24 h at room temperature by using the '$HClO_4$·SiO_2' reagent system. Likewise, trityl ethers are readily cleaved to the corresponding alcohols in good to excellent yields within 2–3 h at room temperature. Work-up involves merely filtration of the reagent followed by purification of the crude product.

Keywords: Isopropylidene acetals; Trityl ether; $HClO_4$–SiO_2

Selective protection and deprotection of functional groups is extremely useful in organic synthesis. Isopropylidene acetals (acetonides) have been widely used for the protection of 1,2- and 1,3-diols in carbohydrate and nucleoside chemistry.[1] Hydrolysis of terminal isopropylidene acetals in the presence of internal ones is often needed in a synthetic sequence. There are various types of protic and Lewis acids that have been used for the deprotection of isopropylidene acetals such as aq H_2SO_4,[2a] Dowex acidic ion-exchange resin in CH_3OH–H_2O (9:1),[2b] trifluoroacetic acid,[2c] $Zn(NO_3)_2$·$6H_2O$,[3a] and $BiCl_3$.[3b] Clearly, some of the protic acids are strongly acidic, and because water is invariably used along with many of these reagents, sometimes nonselective hydrolysis is also observed leading to decreased yields of the desired products. Interestingly, thiourea[4] has been reported as a reagent for this purpose and this can be considered as a somewhat neutral reagent. Identification of these various reagents was the result of investigations aimed at improving the efficiency of deprotections of terminal isopropylidene groups in terms of cost, ease of handling of the reagent, mildness, and duration of the reactions, and also ease of work-up. There have also been attempts to introduce supported reagents like $FeCl_3$·$6H_2O$/SiO_2[5a] and $NaHSO_4$·SiO_2,[5b] due to ease of work-up and environmental factors.

Likewise, trityl ethers have also served as excellent protecting groups in organic synthesis, especially in carbohydrate chemistry,[1] and consequently their deprotection is also reported using different reagents. As applicable for isopropylidene deprotections, both protic and Lewis acids such as formic acid,[6a] trifluoroacetic acid,[6b] BCl_3,[7a] and $Yb(OTf)_3$[7b] have been reported for the deprotection of trityl ethers. Recently, deprotection of trityl ethers has been reported[8a] by using column chromatography where the silica gel was saturated with 5% trifluoroacetic acid. More recently, deprotection of trityl ethers has been reported[8b] by using $NaHSO_4$·SiO_2. Clearly, the last two procedures fall in the category of supported reagents.

Recently we have reported[9a] that $HClO_4$ supported on silica gel ($HClO_4$·SiO_2)[10] acts as an efficient and mild reagent for both the Ferrier reaction of tri-*O*-acetyl glucal, and the conversion of D-glucose and D-galactose into a chiral furan diol. In these cases, the yields are excellent. In continuation of these studies,[9] we now report that $HClO_4$·SiO_2 effectively deprotects terminal isopropylidene groups and trityl ethers to form the desired products

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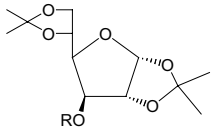
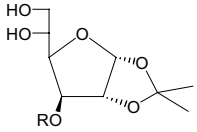
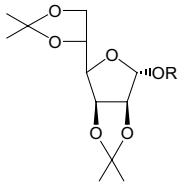
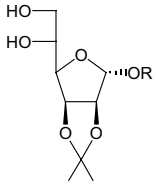
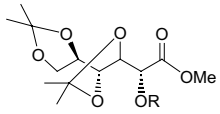
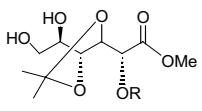
in good to excellent yields. Deprotection of the isopropylidene group is based on transacetalization, as CH_3OH is used as a solvent. The reactions were also performed in other solvents such as CH_2Cl_2 and CH_3CN; however, they were found to be extremely sluggish in CH_3CN whereas no reaction was observed in CH_2Cl_2. Likewise, during the deprotection of trityl ethers, CH_3OH acts as a nucleophile to trap the generated trityl cation. Under these conditions, several functional groups such as benzoyl, *p*-nitrobenzoyl, tosyl, *tert*-butyldimethylsilyl, allyl, *p*-methoxyphenyl, thiophenyl, and *p*-methoxybenzyl all remain unaffected. The work-up simply involves filtration of the reagent followed by evaporation of the solvent and purification of the product by chromatography. Further, the reactions could also be performed at relatively larger scale (30–40 mmol) with practically no change in yields or the reaction time. Thus, compound **16**, which is needed for other purposes, is routinely prepared in our laboratory by deprotecting acetonide **2** on a large scale using $HClO_4{\cdot}SiO_2$ and we find it very convenient because the method avoids any aqueous work-up. Stirring a solution of the substrate (a trityl ether or an acetonide) in CH_3OH with silica gel for several days did not permit any appreciable cleavage indicating that $HClO_4$ is necessary to be used along with silica gel for the efficient deprotections. Our results are summarized in Tables 1 and 2. All products were characterized by ^1H NMR, ^{13}C NMR, and mass spectral data and compared with the literature data where available.

This supported reagent system is very cheap, environmentally friendly and easy to handle. Furthermore, because the work-up involves merely filtration of the reagent followed by purification, it is expected that these methods will find application in organic synthesis.

Table 1. Deprotection of isopropylidene acetals by $HClO_4{\cdot}SiO_2$[a]

Diisopropylidene	Product 1,2-diol	Time (h)	Yield (%)
			
1: R = H[11]	**15**[12]	10	95
2: R = Bn[13]	**16**[13]	10	90
3: R = Allyl[14]	**17**[14]	6	85
4: R = Ms[15]	**18**[16]	12	90
5: R = Ts[15]	**19**[5b]	20	85
6: R = Bz	**10**[17]	8	90
7: R = PNB	**21**	10	85
8: R =TBDMS[5a]	**22**[3b]	24	85
9: R = PMB[18]	**23**[18]	10	86
			
10: R = Bn[19]	**24**[19]	20	88
11: R = Bz[20]	**25**[21]	20	85
			
12: R = H[22]	**26**[3a]	24	87
13: R = Bz	**27**	24	85
14: R = Ts	**28**	24	85

[a] For compounds **1**–**11** the amount of reagent was 100 mg per 100 mg of substrate; for **12**–**14**, 200 mg of the reagent was used per 100 mg of substrate.

1. Experimental

1.1. General methods

^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on JEOL JNM-LA 400 FT NMR spectrometer in a solution of $CDCl_3$ as a solvent using Me_3Si as an internal standard. Infrared spectra were recorded on a Bruker Vector 22 FT-IR spectrometer. Elemental analyses were determined using Themoquest CE-instruments EA-1110 automatic elemental analyzer. Mass spectra were recorded on Microscopic II Triple Quadrupole mass spectrometer using the electrospray technique. Optical rotation values were recorded on Autopol II automatic polarimeter at the wavelength of sodium *d*-line (589 nm) at 25 °C. Thin-layer chromatography was performed on precoated silica gel plates (E-Merck, Germany). Solvents and liquid reagents were purified and dried according to recommended procedures.

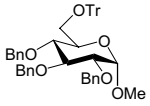
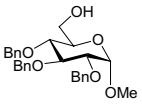
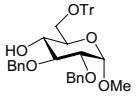
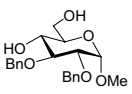
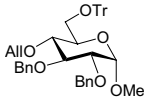
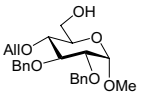
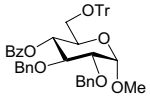
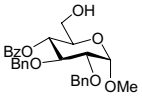
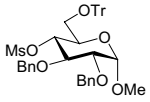
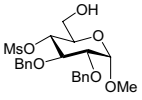
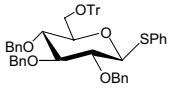
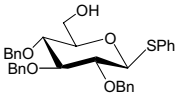
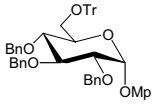
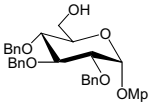
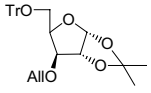
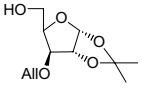
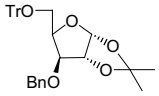
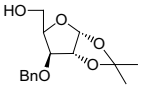
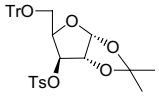
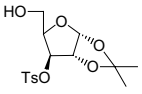
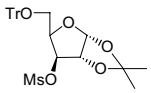
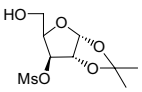
1.2. Preparation of the $HClO_4{\cdot}SiO_2$ reagent system

$HClO_4$ (0.061 mL, as a 70% aqueous solution) was added to a suspension of silica gel (2 g, 200–400 mesh) in Et_2O (20 mL) while swirling. The mixture was concentrated on a rotary evaporator under vacuum. The residue so obtained was heated for 6 h at 100 °C under vacuum, while being magnetically stirred, to obtain $HClO_4{\cdot}SiO_2$ as a free flowing powder.

1.3. Deprotection of isopropylidene acetals

To a solution of an isopropylidene acetal protected compound (100 mg) in CH_3OH (1.5 mL) was added $HClO_4{\cdot}SiO_2$ (amount according to Table 1). The heterogeneous mixture was stirred at room temperature for the appropriate time (Table 1). After completion of the reaction (TLC monitoring), the mixture was filtered and washed with CH_3OH. The combined filtrate was concentrated under vacuum and the residue was purified by column chromatography to obtain the pure 1,2-diol.

Table 2. Deprotection of trityl ethers by $HClO_4{\cdot}SiO_2$[a]

Trityl ether	Time (h)	Product	Yield (%)
 **29**[23]	2	 **40**[24]	92
 **30**[25]	2	 **41**[26]	90
 **31**[25]	2	 **42**	90
 **32**	2	 **43**	85
 **33**	2	 **44**	85
 **34**	2.5	 **45**[27]	89
 **35**	2	 **46**	86
 **36**[28]	2	 **47**[28]	85
 **37**[29]	2	 **48**[29]	90
 **38**[28]	3	 **49**[28]	85
 **39**[30]	2.5	 **50**[31]	87

[a] 100 mg of $HClO_4{\cdot}SiO_2$ was used per 100 mg of substrate.

1.4. Deprotection of trityl ethers

To a solution of a trityl ether (100 mg) in CH_3OH (1.5 mL) was added $HClO_4{\cdot}SiO_2$ (100 mg) and the reaction mixture was stirred at room temperature for the required time (see Table 2). After completion of the reaction (TLC monitoring), the solution was filtered and the filtered solid was washed with CH_3OH. The combined organic solution was concentrated under vacuum and the crude product was purified by column chromatography to obtain the pure detritylated product.

1.5. 3-*O*-Benzoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (6)

To a solution of 1,2:5,6-di-*O*-isopropylidiene-α-D-glucofuranose (**1**, 260 mg, 1 mmol) in dry pyridine (3 mL) was added benzoyl chloride (0.13 mL, 1.1 mmol) and the reaction mixture was stirred at room temperature for 48 h. After completion of the reaction (TLC monitoring), the solution was diluted with CH_2Cl_2, washed with water and brine, dried over Na_2SO_4, and then concentrated under vacuum. The product was purified by column chromatography on silica gel, yielding **6** in 92% yield; $[\alpha]_D$ −3.5 (*c* 4.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ_H 1.28 (s, 3H, C*H*$_3$), 1.32 (s, 3H, C*H*$_3$), 1.43 (s, 3H, C*H*$_3$), 1.56 (s, 3H, C*H*$_3$), 4.09–4.15 (m, 2H, H-6, H-6′), 4.33–4.41 (m, 2H, H-4, H-5), 4.64 (d, 1H, *J* 3.7 Hz, H-2), 5.51 (d, 1H, *J* 2.7 Hz, H-3), 5.96 (d, 1H, *J* 3.6 Hz, H-1), 7.43–7.69 (m, 3H, $OCOC_6H_5$), 8.02–8.17 (m, 2H, $OCOC_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 25.1, 26.1, 26.6, 26.7, 67.1, 72.5, 76.5, 79.8, 83.3, 105.0, 109.3, 112.3, 128.4, 128.8, 129.6, 130.5, 133.4, 134.5, 165.1; IR (CH_2Cl_2) 3022, 1742 cm^{-1}; ESIMS (*m*/*z*): 387 $[M+Na]^+$, 281 $[(M-84)+1]^+$. Anal. Calcd for $C_{19}H_{24}O_7$ (364.15): C, 62.63; H, 6.64. Found: C, 62.66; H, 6.61.

1.6. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-*p*-nitrobenzoyl-α-D-glucofuranose (7)

To a solution of 1,2:5,6-di-*O*-isopropylidiene-α-D-glucofuranose (**1**, 260 mg, 1 mmol) in dry CH_2Cl_2 (3 mL) was added *p*-nitrobenzoyl chloride (204 mg, 1 mmol) and triethylamine (0.15 mL, 1 mmol). The reaction mixture was stirred at room temperature for 48 h. After completion of the reaction (TLC monitoring) the solution was diluted with CH_2Cl_2 and washed with water and brine, dried over Na_2SO_4 and then concentrated under vacuum. The crude product was purified by column chromatography on silica gel to give the product in 72% yield as a syrup; $[\alpha]_D$ −50.7 (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ_H 1.26 (s, 3H, C*H*$_3$), 1.34 (s, 3H, C*H*$_3$), 1.41 (s, 3H, C*H*$_3$), 1.57 (s, 3H, C*H*$_3$), 4.07–4.09 (dd, 1H, *J* 4.2, 8.6 Hz, H-6), 4.09–4.14 (dd, 1H, *J* 5.1,

8.5 Hz, H-6′), 4.30–4.36 (m, 2H, H-4, H-5), 4.65 (d, 1H, *J* 3.9 Hz, H-2), 5.53 (d, 1H, *J* 2.4 Hz, H-3), 5.97 (d, 1H, *J* 3.6 Hz, H-1), 8.19–8.22 (m, 2H, $OCOC_6H_5$), 8.31–8.33 (2H, m, $OCOC_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 25.1, 25.2, 26.2, 26.7, 28.9, 67.5, 72.5, 76.1, 77.6, 79.9, 83.3, 105.1, 109.6, 112.5, 123.7, 130.8, 134.9, 150.8, 163.4; IR (CH_2Cl_2): 2988, 1734, 1607, 1531 cm^{-1}; ESIMS (*m*/*z*): 432 $[M+Na]^+$, 325 $[M-84]^+$. Anal. Calcd for $C_{19}H_{23}NO_9$ (409.14): C, 55.74; H, 5.66; N, 3.42. Found: C, 55.67, H, 5.61; N, 3.39.

1.7. 2-*O*-Benzoyl-3,4:5,6-di-*O*-isopropylidene-D-gluconate (13)

Benzoate **13** was synthesized from **12** following the procedure used for the preparation of **6**. The product was obtained in 92% yield as a yellow syrup; $[\alpha]_D$ +2.0 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.29 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 3.92–3.99 (m, 2H, H-4, H-6), 4.13 (m, 2H, H-5, H-6′), 4.60 (dd, 1H, *J* 2.2, 7.8 Hz, H-3), 5.62 (d, 1H, *J* 2.0 Hz, H-2), 7.45–7.49 (m, 1H, $OCOC_6H_5$), 7.58–7.62 (m, 2H, $OCOC_6H_5$), 8.10–8.12 (m, 2H, $OCOC_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 25.1, 26.6, 26.8, 27.2, 52.7, 67.6, 71.2, 76.6, 77.1, 79.4, 109.9, 110.5, 128.5, 129.2, 129.9, 133.5, 165.7, 168.1; IR (CH_2Cl_2): 3025, 1747, 1730 cm^{-1}; ESIMS (*m*/*z*): 417 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{26}O_8$ (394.16): C, 60.90; H, 6.64. Found: C, 60.83; H, 6.61.

1.8. 3,4:5,6-Di-*O*-isopropylidene-2-*O*-*p*-toluenesulfonyl-D-gluconate (14)

To a solution of compound **12** (289 mg, 1 mmol) in pyridine (3 mL), was added *p*-toluenesulfonyl chloride (209.72 mg, 1.1 mmol). The reaction mixture was stirred for 24 h at room temperature. After completion (TLC monitoring) the solution was diluted with CH_2Cl_2, washed with water and brine, dried over Na_2SO_4, and concentrated under vacuum. The product was purified by silica gel column chromatography to yield **14** in 91% yield as a yellow syrup; $[\alpha]_D$ +2.0 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.33, (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 2.44 (s, 3H, $OCOC_6H_4$–*p*CH_3), 3.69 (s, 3H, CO_2CH_3), 3.83–4.01 (m, 2H, H-4, H-6), 4.04–4.19 (m, 2H, H-5, H-6′), 4.44–4.46 (dd, 1H, *J* 2.0, 7.1 Hz, H-3), 5.16 (d, 1H, *J* 2.0 Hz, H-1), 7.31–7.36 (m, 2H, $OCOC_6H_4$–*p*CH_3), 7.82–7.87 (m, 2H, $OCOC_6H_4$–*p*CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 21.5, 25.2, 25.4, 26.3, 27.2, 52.6, 57.9, 58.1, 63.5, 75.6, 78.5, 109.6, 110.2, 128.2, 129.6, 132.8, 145.2, 167.3; IR (CH_2Cl_2) 1745 cm^{-1}; ESIMS (*m*/*z*): 467 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{28}O_9S$ (444.15): C, 54.04; H, 6.35; S, 7.85. Found: C, 54.00; H, 6.21; S, 7.87.

1.9. 1,2-*O*-Isopropylidene-3-*O*-*p*-nitrobenzoyl-α-D-glucofuranose (21)

The product was obtained in 85% yield as a syrup; $[\alpha]_D$ −14.9 (*c* 0.9, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.34 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 3.74–3.89 (m, 3H, H-5, H-6, H-6′), 4.31 (dd, 1H, *J* 2.7, 8.8 Hz, H-4), 4.70 (d, 1H, *J* 3.6 Hz, H-2), 5.56 (d, 1H, *J* 2.7 Hz, H-3), 5.99 (d, 1H, *J* 3.7 Hz, H-1), 8.20–8.31 (m, 4H, $OCOC_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 26.1, 26.5, 29.6, 63.9, 68.4, 76.7, 78.9, 82.9, 104.9, 112.5, 123.7, 134.6, 150.9, 164.2; IR (CH_2Cl_2) 3428, 2993, 1729, 1609, 1530 cm^{-1}; ESIMS (*m*/*z*): 756 $[2M+18]^+$, 387 $[M+18]^+$, 370 $[M+H]^+$. Anal. Calcd for $C_{16}H_{19}NO_9$ (369.11): C, 52.03; H, 5.19; N, 3.79. Found: C, 52.00; H, 5.15; N, 3.69.

1.10. 2-*O*-Benzoyl 3,4-*O*-isopropylidene-D-gluconate (27)

The product was obtained in 85% yield as a yellow syrup; $[\alpha]_D$ +7.8 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.39 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 3.63 (m, 1H, H-6), 3.78 (s, 3H, CO_2CH_3), 3.80–3.85 (m, 2H, H-5, H-6′), 3.96–3.99 (dd, 1H, *J* 7.6, 7.3 Hz, H-4), 4.67 (dd, 1H, *J* 2.2, 7.3 Hz, H-3), 5.61 (d, 1H, *J* 2.2 Hz, H-2), 7.41–7.45 (m, 2H, $OCOC_6H_5$), 7.52–7.58 (m, 1H, $OCOC_6H_5$), 8.10 (m, 2H, $OCOC_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C: 26.8, 27.3, 52.7, 63.8, 71.7, 72.9, 76.1, 78.6, 110.4, 128.5, 129.1, 130.0, 133.6, 166.0, 168.3; IR (CH_2Cl_2) 3530, 1747, 1714 cm^{-1}; ESIMS (*m*/*z*): 377 $[M+Na]^+$. Anal. Calcd for $C_{17}H_{22}O_8$ (354.13): C, 57.62; H, 6.26. Found: C, 57.55; H, 6.23.

1.11. 3,4-*O*-Isopropylidene-2-*O*-*p*-toluenesulfonyl-D-gluconate (28)

The product was obtained in 85% yield as a syrup; $[\alpha]_D$ +6.7 (*c* 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.34 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 2.45 (s, 3H, $OCOC_6H_4$–*p*CH_3), 3.64 (m, 1H, H-6), 3.68 (s, 3H, CO_2CH_3), 3.75–3.79 (m, 1H, H-5), 3.82 (dd, 1H, *J* 3.4, 11.5 Hz, H-6′), 4.00 (dd, 1H, *J* 7.3, 7.1 Hz, H-4), 4.53 (dd, 1H, *J* 2.2, 7.8 Hz, H-3), 5.27 (d, 1H, *J* 2.0 Hz, H-2), 7.35 (d, 2H, *J* 8.3 Hz, $OCOC_6H_4$–*p*CH_3), 7.85 (d, 2H, *J* 8.0 Hz, $OCOC_6H_4$–*p*CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 21.6, 26.2, 27.1, 52.7, 57.9, 58.2, 63.4, 75.6, 78.5, 110.3, 128.1, 129.7, 132.8, 145.3, 167.2; IR (CH_2Cl_2) 3540, 1746, 1341 cm^{-1}; ESIMS (*m*/*z*): 427 $[M+Na]^+$. Anal. Calcd for $C_{17}H_{24}O_9S$ (404.11): C, 50.49; H, 5.98; S, 7.93. Found: C, 50.37; H, 5.89; S, 7.88.

1.12. Methyl 4-*O*-benzoyl-2,3-di-*O*-benzyl-6-*O*-trityl-α-D-glucopyranoside (32)

This compound was synthesized from **30** by the same procedure used for the preparation of **6**. The product

was obtained in 92% yield as a syrup; $[\alpha]_D$ +8.0 (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ_H 3.26–3.36 (m, 2H, H-6, H-6′), 3.42 (s, 3H, OCH_3), 3.52–3.57 (m, 2H, H-2, H-5), 3.67–3.79 (m, 2H, H-3, H-4), 4.66 (d, 1H, *J* 3.7 Hz, H-1), 4.69 (d, 1H, *J* 11.0 Hz, $OCH_2C_6H_5$), 4.73 (d, 1H, *J* 11.2 Hz, $OCH_2C_6H_5$), 4.77 (d, 1H, *J* 11.5 Hz, $OCH_2C_6H_5$), 4.95 (d, 1H, *J* 11.5 Hz, $OCH_2C_6H_5$), 7.13–7.99 (m, 30H, $3\times OC(C_6H_5)$, $2\times OCH_2C_6H_5$, COC_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 55.1, 63.8, 71.5, 73.1, 75.6, 78.8, 79.4, 97.9, 127.0, 127.8, 127.9, 128.0, 128.4, 128.5, 128.7, 138.1, 143.8; IR (CH_2Cl_2) 1735 cm^{-1}; ESIMS (*m*/*z*): 738 $[M+18]^+$. Anal. Calcd for $C_{47}H_{44}O_7$ (720.31): C, 78.31; H, 6.15. Found: C, 78.35; H, 6.10.

1.13. Methyl 2,3-di-*O*-benzyl-4-*O*-methanesulfonyl-6-*O*-trityl-α-D-glucopyranoside (33)

To a solution of compound **30** (616 mg, 1 mmol) in dry CH_2Cl_2 at 0 °C, was added triethylamine (0.15 mL, 1.5 mmol) and methanesulfonyl chloride (0.09 mL, 1.2 mmol). The reaction mixture was stirred for 1 h and after completion of reaction (TLC monitoring) aq $NaHCO_3$ was added. The organic layer was separated, washed with water, brine, dried over Na_2SO_4, and concentrated under vacuum. The product was purified by silica gel column chromatography to give **33** in 82% yield as a syrup; $[\alpha]_D$ +35.5 (*c* 0.7, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ_H 2.79 (s, 3H, SO_2CH_3), 3.17 (dd, 1H, *J* 7.6, 7.3 Hz, H-6), 3.38 (s, 3H, OCH_3), 3.44 (dd, 1H, *J* 7.3 Hz, H-6′) 3.58 (dd, 1H, *J* 3.4, 9.8 Hz, H-2), 3.71–3.75 (m, 1H, H-5), 3.91–4.06 (dd, 1H, *J* 9.3 Hz, H-4), 4.45–4.50 (t, 1H, *J* 8.8 Hz, H-3), 4.65 (d, 1H, *J* 3.4 Hz, H-1), 4.61–4.64 (m, 2H, $OCH_2C_6H_5$), 4.74 (d, 1H, *J* 12.0 Hz, $OCH_2C_6H_5$), 5.08 (d, 1H, *J* 11.2 Hz, $OCH_2C_6H_5$), 7.26–7.33 (m, 25H, $2\times OCH_2C_6H_5$, $OC(C_6H_5)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 38.2, 55.5, 60.3, 69.6, 73.3, 75.7, 76.7, 77.6, 78.5, 80.1, 97.7, 127.2, 127.8, 127.9, 128.3, 128.5, 128.6, 137.8, 146.8; IR (CH_2Cl_2) 1125 cm^{-1}; ESIMS (*m*/*z*): 712 $[M+18]^+$, 695 $[M+1]^+$. Anal. Calcd for $C_{41}H_{42}O_8S$ (694.26): C, 70.87; H, 6.09; S, 4.61. Found: C, 70.77; H, 5.99; S, 4.59.

1.14. Phenyl 2,3,4-tri-*O*-benzyl-1-thio-6-*O*-trityl-β-D-glucopyranoside (34)

Phenyl 1-thio-β-D-glucopyranoside was prepared according to the literature procedure.[32] A solution of this compound (400 mg, 1.48 mmol) and trityl chloride (380 mg, 1.35 mmol) in pyridine was stirred at room temperature for 24 h. The mixture was poured into water and extracted with CH_2Cl_2. The combined extract was washed with water, dried, and concentrated in vacuum to give crude phenyl 1-thio-6-*O*-trityl-β-D-glucopyranoside (637 mg). To a mixture of this intermediate and NaH (172 mg, 7.15 mmol) in DMF (4 mL) was added benzyl bromide (0.44 mL, 3.72 mmol) at 0 °C and the resulting mixture was stirred at room temperature for 5 h. Excess NaH was destroyed by CH_3OH and the reaction mixture was poured into water and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, and concentrated. The crude product was purified by silica gel column chromatography to give **34** in 70% yield as a yellow paste; $[\alpha]_D$ −12.9 (*c*, 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ_H 3.26 (m, 1H, H-5), 3.45 (dd, 1H, *J* 9.5 Hz, H-2), 3.58–3.69 (m, 3H, H-6, H-6′,H-4), 3.74 (dd, 1H, *J* 9.5 Hz, H-3), 4.31 (d, 1H, *J* 10.2 Hz, H-1), 4.56–4.93 (m, 6H, $OCH_2C_6H_5$), 7.16–7.52 (m, 35H, $3\times OC(C_6H_5)$, $3\times OCH_2C_6H_5$, SC_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 62.4, 72.1, 75.0, 75.4, 76.0, 76.7, 78.8, 80.8, 86.5, 86.8, 87.3, 126.9, 127.4, 127.6, 127.8, 128.1, 128.2, 128.4, 128.5, 128.8, 128.9, 131.9, 133.8, 137.6, 138.1, 138.3; IR (CH_2Cl_2) 1122 cm^{-1}; ESIMS (*m*/*z*): 803 $[M+18]^+$. Anal. Calcd for $C_{52}H_{48}O_5S$ (784.32): C, 79.56; H, 6.16; S, 4.08. Found: C, 78.93; H, 6.12; S, 4.12.

1.15. *p*-Methoxyphenyl 2,3,4-tri-*O*-benzyl-6-*O*-trityl-α-D-glucopyranoside (35)

p-Methoxyphenyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside was prepared according to the literature procedure.[33] To a solution of this compound (465 mg, 1 mmol) in CH_3OH (4 mL) was added $NaOCH_3$ to maintain the pH of the solution at 10. After stirring the solution for 6 h at room temperature, it was neutralized by addition of Dowex-50 (H^+). The mixture was filtered and concentrated under vacuum. The residue was selectively tritylated and benzylated using the same procedure employed for the synthesis of **34**. Compound **35** was obtained in 72% yield as a yellow syrup; $[\alpha]_D$ +63.3 (*c*, 0.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ_H 3.14 (m, 1H, H-5), 3.45 (dd, 1H, *J* 10.2 Hz, H-2), 3.55 (m, 2H, H-3, H-6), 3.77 (s, 3H, OCH_3), 3.95 (m, 1H, H-6′), 4.23 (t, 1H, *J* 9.3 Hz, H-4), 4.35 (dd, 1H, *J* 11.0 Hz, $OCH_2C_6H_5$), 4.69–4.74 (m, 5H, $OCH_2C_6H_5$), 5.48 (d, 1H, *J* 3.4 Hz, H-1), 6.83–7.45 (m, 34H, $3\times OCH_2C_6H_5$, OC_6H_4–*p*OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 55.6, 62.7, 65.4, 70.6, 73.5, 74.6, 76.7, 79.5, 86.3, 95.5, 114.5, 118.2, 126.9, 127.0, 127.7, 127.9, 128.0, 128.3, 128.6, 128.8, 143.9; IR (CH_2Cl_2) 1132 cm^{-1}; ESIMS (*m*/*z*): 816 $[M+18]^+$. Anal. Calcd for $C_{53}H_{50}O_7$ (798.36): C, 79.67; H, 6.31. Found: C, 79.31; H, 6.18.

1.16. Methyl 4-*O*-allyl-2,3-di-*O*-benzyl-α-D-glucopyranoside (42)

The product was obtained in 90% yield as a white solid; mp 77–78 °C; $[\alpha]_D$ +40.9 (*c* 1, $CHCl_3$); lit.[26] mp 76–79 °C; $[\alpha]_D$ +39.2 (*c* 1, $CHCl_3$); ^1H NMR (400 MHz,

$CDCl_3$): δ_H 3.37 (s, 3H, OCH_3), 3.35–3.40 (m, 1H, H-4), 3.45 (dd, 1H, *J* 3.6, 9.5 Hz, H-2), 3.60–3.64 (m, 1H, H-5), 3.71 (dd, 1H, *J* 4.2, 11.7 Hz, H-6), 3.80 (dd, 1H, *J* 2.9, 11.7 Hz, H-6′), 3.93 (dd, 1H, *J* 9.0, 9.5 Hz, H-3), 4.11–4.15 (m, 1H, =CH–CH_2), 4.31–4.35 (m, 1H, =CH–CH_2), 4.56 (d, 1H, *J* 3.6 Hz, H-1), 4.64 (d, 1H, *J* 12.2 Hz, $OCH_2C_6H_5$), 4.78 (d, 1H, *J* 11.0 Hz, $OCH_2C_6H_5$), 4.79 (d, 1H, *J* 12.2 Hz, $OCH_2C_6H_5$), 4.93 (d, 1H, *J* 11.0 Hz, $OCH_2C_6H_5$), 5.14–5.29 (m, 2H, –CH=CH_2), 5.86–5.93 (m, 1H, –CH=CH_2), 7.25–7.39 (m, 10H, $2\times OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 55.2, 61.9, 70.6, 73.4, 73.7, 75.7, 77.5, 79.8, 81.7, 98.2, 117.1, 127.6, 127.9, 128.0, 128.3, 128.4, 134.7, 138.1, 138.7; IR (CH_2Cl_2) 3423 cm^{-1}; ESIMS (*m*/*z*): 437 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{30}O_6$ (414.20): C, 69.54; H, 7.30. Found: C, 69.51; H, 7.24.

1.17. Methyl 4-*O*-benzoyl-2,3-di-*O*-benzyl-α-D-glucopyranoside (43)

The product was obtained in 85% yield as a syrup; $[\alpha]_D$ +77.5 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.67 (br s, 1H, O*H*), 3.42 (s, 3H, OCH_3), 3.57–3.77 (m, 4H, H-2, H-5, H-6, H-6′), 4.12 (t, 1H, *J* 9.3 Hz, H-3), 4.66 (d, 1H, *J* 3.2 Hz, H-1), 4.69 (d, 2H, *J* 11.0 Hz, $OCH_2C_6H_5$), 4.81(d, 1H, *J* 12.2 Hz, $OCH_2C_6H_5$), 4.85 (d, 1H, *J* 11.2 Hz, $OCH_2C_6H_5$), 5.14 (t, 1H, *J* 9.5 Hz, H-4), 7.13–7.99 (m, 15H, $OCH_2C_6H_5$, $OCOC_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 55.4, 61.1, 69.7, 71.1, 73.6, 75.5, 78.8, 79.4, 98.3, 127.5, 127.9, 128.0, 128.2, 129.1, 129.9, 133.5, 137.9, 138.1, 166.6; IR (CH_2Cl_2) 3502, 2917, 1732, 1557, 1450 cm^{-1}; ESIMS (*m*/*z*): 496 $[M+18]^+$, 479 $[M+1]^+$, 447 $[M-31]^+$. Anal. Calcd for $C_{28}H_{30}O_7$ (478.20): C, 70.28; H, 6.32. Found: C, 70.31; H, 6.32.

1.18. Methyl 2,3-di-*O*-benzyl-4-*O*-methanesulfonyl-α-D-glucopyranoside (44)

The product was obtained in 85% yield as a syrup; $[\alpha]_D$ +6.9 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.79 (s, 3H, SO_2CH_3), 3.39 (s, 3H, OCH_3), 3.58 (dd, 1H, *J* 3.7, 9.5 Hz, H-2), 3.71–3.74 (m, 1H, H-5), 3.79 (br s, 1H, O*H*), 3.91 (dd, 1H), 4.02 (t, 1H, *J* 9.3 Hz, H-3), 4.45 (t, 1H, *J* 9.8 Hz, H-4), 4.62–4.69 (m, 2H, $OCH_2C_6H_5$), 4.64 (d, 1H, *J* 3.7 Hz, H-1), 4.74 (d, 1H, *J* 12.0 Hz, $OCH_2C_6H_5$), 5.07 (d, 1H, *J* 11.2 Hz, $OCH_2C_6H_5$), 7.29–7.34 (m, 10H, $2\times OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 38.2, 55.5, 60.3, 62.2, 69.6, 73.3, 75.7, 77.6, 78.5, 80.1, 97.7, 127.8, 127.9, 128.3, 128.5, 128.6; IR (CH_2Cl_2) 3462, 2925, 1745, 1562, 1451 cm^{-1}; ESIMS (*m*/*z*): 470 $[M+18]^+$, 453 $[M+1]^+$, 422 $[(M-31)+1]^+$. Anal. Calcd for $C_{22}H_{28}O_8S$ (452.15): C, 58.39; H, 6.24; S, 7.09. Found: C, 58.28; H, 6.21; S, 6.98.

1.19. *p*-Methoxyphenyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (46)

The product was obtained in 87% yield as a foam; $[\alpha]_D$ + 64 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.62–3.72 (m, 3H, H-2, H-3, H-6), 3.78–3.86 (m, 1H, H-5, H-6′), 4.18 (t, 1H, *J* 9.3 Hz, H-4), 4.66–4.71 (m, 2H, $OCH_2C_6H_5$), 4.79 (d, 1H, *J* 11.9 Hz, $OCH_2C_6H_5$), 4.89–4.93 (m, 2H, $OCH_2C_6H_5$), 5.29 (d, 1H, *J* 3.6 Hz, H-1), 6.81 (d, 2H, *J* 9.3 Hz, OC_6H_4–*p*OCH_3), 6.96 (d, 2H, *J* 9.0 Hz, OC_6H_4–*p*OCH_3), 7.28–7.40 (m, 15H, $OCH_2C_6H_5$); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 55.6, 61.6, 71.5, 73.3, 75.1, 75.8, 76.7, 79.9, 81.8, 96.5, 114.5, 118.3, 127.7, 127.9, 128.0, 128.4, 128.5, 138.1, 138.7, 150.6, 155.1; IR (CH_2Cl_2) 3429 cm^{-1}; ESIMS (*m*/*z*): 574 $[M+18]^+$. Anal. Calcd for $C_{34}H_{36}O_7$ (556.25): C, 73.36; H, 6.52. Found: C, 72.93; H, 6.45.

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Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.carres.2005.04.005.

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