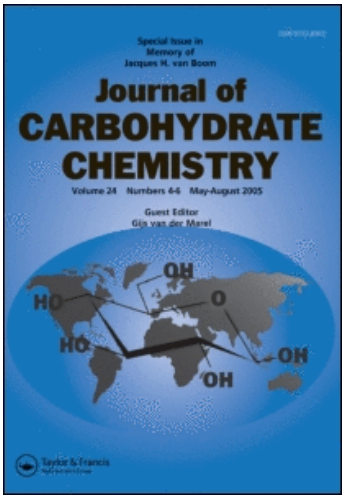

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RAPID CARBOHYDRATE PROTECTING GROUP MANIPULATIONS ASSISTED BY MICROWAVE DIELECTRIC HEATING

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ABSTRACT

The protocols for oligosaccharide synthesis are often tedious due to extended synthetic routes and reaction times. We herein describe methods assisted by microwave dielectric heating, which enable very short reaction times and high yields for the introduction and removal of eleven of the most commonly used protecting groups in carbohydrate syntheses. Several examples are reported, where solid supported reagents in combination with microwave dielectric heating have been used. This results in both faster and easier synthesis and purification.

INTRODUCTION

The methods needed to produce complex oligosaccharides are often tedious and complex, irrespective of whether they involve synthesis or isolation from natural sources. However, since carbohydrates play an important role in a vast array of biological processes, and there are advantages of carbohydrate-based drugs such as low toxicity and immunogenicity, the interest in carbohydrates as drug candidates is still high.[1] In the development of new chemical entities today, there is a need for faster and simpler methods for organic synthesis in general and for carbohydrate synthesis in particular. Since 1986 microwave irradiation has become an increasingly popular method for accelerating synthetic transformation in the laboratory.[2] This technology offers a clean, effective and convenient method of heat-

ing, which often results in higher yields and almost always shorter reaction times. Some of the applications that have been published lately include palladium assisted cross-coupling chemistry,[3] cyclisation reactions[4] and multi-component reactions.[5] Carbohydrate chemistry assisted by microwave dielectric heating has so far been described in a very limited number of publications.[6] There has been a small number of publications dealing with protecting group chemistry but so far most of these publications are reports of deprotection of different protecting groups using solvent free techniques.[7] We herein describe methods for fast and high yielding protection and deprotection of hydroxyl functionalities assisted by microwave dielectric heating. In several cases a comparison is made with results obtained with conventional methods described in the literature.

RESULTS AND DISCUSSION

Eleven common protecting groups were chosen representing acyl-, alkyl-, silyl-, and acetal derivatives. As carbohydrate model compounds the monosaccharides 1,2;5,6-di-*O*-isopropylidene-α-D-glucopyranose (**1**) and methyl α-D-glucopyranoside (**3**) were selected. In this study a Smithsynthesizer from Personal Chemistry was used. This microwave-based synthesizer has a single mode cavity with temperature regulation and pressure control, which means, that temperature runaway and explosion risk are avoided. It should be noticed that the reaction condition is not expressed by the power generated from the magnetron as for most microwave-assisted reactions published. All the data on the introduction of the various protecting groups are summarized in Table 1. The yields are all isolated yields after silica gel chromatography. However, most of the reactions were "one-spot" TLC-reactions, and a simple washing procedure (or in the case of solid-supported reagents a simple filtration) gave products in very high yields and sufficiently pure to be used in subsequent reactions.

Acylations (Table 1, Entries 1–10, Schemes 1 and 2)

Compound **1** was acylated with acetyl chloride, chloroacetyl chloride, pivaloyl chloride and benzoyl chloride together either with a conventional base, pyridine, or with *N,N*-(diisopropyl)aminoethylpolystyrene (PS-DIEA) or *N*-(methylpolystyrene)-4-(methylamino)pyridine (PS-DMAP) to give the 3-*O*- protected compounds **1a**-**1d** in good yields in less than 20 minutes. The use of solid supported reagent in these reactions resulted in a slightly slower reaction but still fast compared to conventional methods. Of special interest are the entries regarding the formations of pivaloyl esters (Entries 5–8). Due to the steric bulk of the pivaloyl group, these are often very slow reactions using conventional methods. However, utilizing microwave heating pivaloate formation (even multiple, Entry 8) are in the same time range as acetate or benzoate formation.

With compound **1** as starting material a byproduct was formed in about 25% yield during benzoylation and pivaloylation with pyridine as base. This was shown

Table 1. Protection

	Product	Reagent	Base	Temp. (°C)	Time/Yield (min)/(%)	Ratio 1:2[a]	Convent. Methods Time/Yield/Temp. (min)/(%)/(°C)
1	**1a**	AcCl	Pyridine	170	12/80		n.d./81/60[9]
2	**1a**	AcCl	PS-DIEA	165	20/66		—
3	**1a**	AcCl	PS-DMAP	180	15/85		—
4	**1b**	ClAcCl	Pyridine	100	8/95		—
5	**1c** + **2c**	PivCl	Pyridine	170	15/85	3:1	n.d./77/60[9]
6	**1c**	PivCl	PS-DIEA	160	20/79		—
7	**1c**	PivCl	PS-DMAP	180	15/88		300/88/rt[19]
8	**3a**	PivCl	pyridine	160	10/68		2160/82/rt[11]
9	**1d** + **2d**	BzCl	Pyridine	170	10/96	3:1	10/95/rt[b,10]
10	**1d**	BzCl	PS-DMAP	170	15/89		—
11	**1e**	AllBr	NaH	190	1/88		720/87/rt[12]
12	**1f**	BnCl	NaH	190	1/95		—
13	**1f**	BnBr	NaH	180	1/96		120/82/50[13]
14	**1f**	BnCl	KOH	150	2/98		300/82/reflux[14]
15	**1f**	BnBr	Ag_2O	190	20/68		5640/90/rt[15]
16	**1g**	*p*MBnBr	KOH	160	5/90		120/94/rt[16]
17	**1h**	*o*NO_2BnBr	NaH	180	2/94		300/29/rt[b,17]
18	**1i** + **2i**	Bu^tMe_2SiCl	Imidazole	200	10/94	3:1	120/90/rt[b,18]
19	**1i** + **2i**	Bu^tMe_2SiCl	PS-DMAP	180	15/83	3:1	11520/65/rt[19]
20	**1j**	BSA	—	190	5/93		—
21	**3b**	BSA	—	180	10/70		—
22	**3c**	$PhCHBr_2$	PS-DMAP	170	5/83		—

[a] Determined by NMR.
[b] Not the same reagents.

to be 6-*O*-benzoyl(pivaloyl)-1,2;3,5-di-*O*-isopropylidene-α-D-glucopyranose (**2c** and **2d**) obtained through a 5,6 to 3,5-acetal migration prior to acylation. Acetal migration was not observed for the acetylation and chloroacetylation reactions, indicating that acetylation is too rapid to allow for the acetal rearrangement. This migration, which has been observed earlier under Koenigs-Knorr and halogenation conditions,[8] is probably catalyzed by the formed pyridinium chloride, since irradiation of **1** in pyridine with no acyl chloride added showed no migration. Furthermore, the use of a solid supported base, when the pyridinium chloride formed is bound to the resin and not free in solution, prevented the migration.

Alkylations (Table 1, Entries 11–17, Scheme 1)

With a strong base very short reaction times were needed and excellent yields of products were obtained. Also with a weak base an acceptable yield of product was obtained in about 20 minutes (Entry 15). Most interesting is that the short reaction time permits the use of a strong base even with base-labile starting materials. For example, nitrophenyl groups in the reagent or in the saccharide to be pro-

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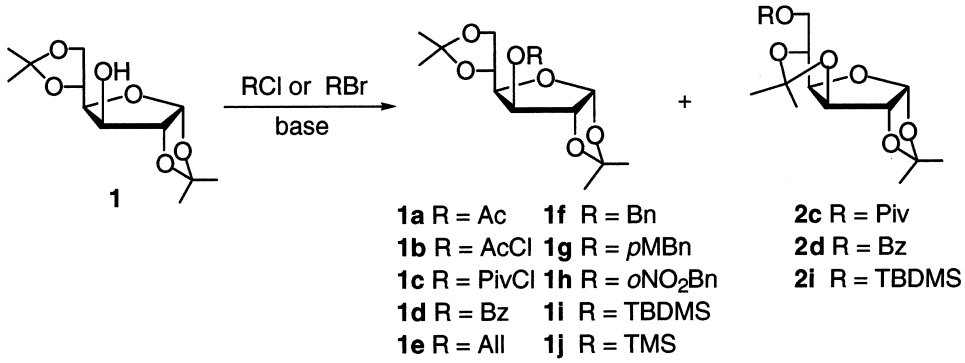


Scheme 1.

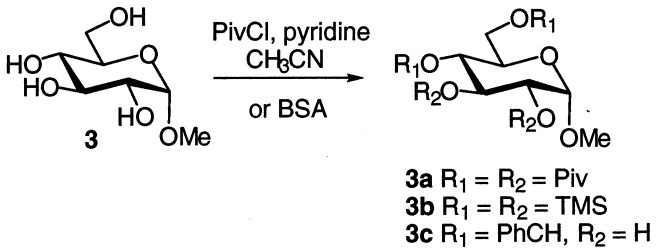
tected most often excludes the use of sodium hydride as base, however, employing microwave heating a very high yield of an *o*-nitrobenzyl protected derivative was obtained (Entry 17).

Silylation (Table 1, Entries 18–21, Schemes 1 and 2)

Tert-Butyldimethylsilyl chloride with pyridine or PS-DMAP was employed for the introduction of TBDMS groups, and for trimethylsilylation *N,O*-bis-(trimethylsilyl)-acetamide (BSA) was used, a reagent which does not require any additional base. Once more, short reaction times and high yields were observed. Additionally, silylation with sterically hindered silyl reagents is the most applicable field for microwave heating resulting in reaction rate enhancements of up to around 700 times as compared to conventional methods (Entry 19). Here, too, acetal migration was observed in compound **1**, but this time the use of a solid supported base did not prevent this side reaction (Entries 18 and 19).

Acetal Formation (Table 1, Entry 22, Scheme 2)

The method developed by Garegg et al.[22] to form benzylidene acetals by using benzal bromide in pyridine under refluxing condition for several hours was



Scheme 2.

Table 2. Deprotection

	Starting Material	Product	Reagent	Temp. (°C)	Time/Yield (min)/(%)
1	**1d**	**1**	Et_3N	150	15/71
2	**1d**	**1**	KCN	120	3/67
3	**4**	**4a**	Et_3N	150	15/78
4	**1i**	**1**	Bu_4NBr/KF	180	2/61
5	**1i**	**glucose**	K10 Clay	150	4/85
6	**1**	**glucose**	K10 Clay	150	3/91
7	**4**	**4b**	K10 Clay	150	2/89
8	**3c**	**3**	Poly-PPTS	150	2/94

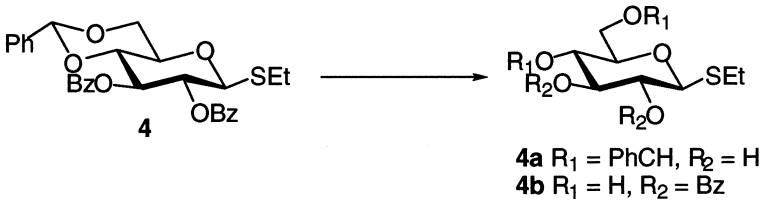
modified. Compound **3** was treated with benzal bromide and PS-DMAP in MeCN to form the 4,6-*O*-benzylidene derivative **3c** in 83% yield after 5 min at 170° C.

Deprotection

For deprotection studies mild condition methods were chosen to see if the extended reaction times often connected with such methods could be shortened by the use of microwave heating. Some solid supported reagents were also tested here. The results are summarized in Table 2.

Deacylation (Table 2, Entries 1–3, Schemes 1 and 3)

The methods described by Tsuzuki et al.[23] and Mori et al.[24] were tried. Compound **1d** and ethyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**4**)[25] were heated at 150 °C for 15 min in a mixture of triethylamine/MeOH/water 1:5:1 to give compound **1** in 71 % yield and compound **4a** in 78% yield. Deacylation of compound **1d** was also achieved using KCN in $EtOH/H_2O$[26] and heating for 3 min at 120 °C to give **1** in 67% yield.



Scheme 3.

Desilylation and Deacetalation (Table 2, Entries 4–8, Schemes 1–3)

There are a number of methods for deprotection of silyl groups under both acidic and basic conditions.[27] For basic conditions, compound **1i** was treated with Bu_4NBr and KF for 2 min at 180 °C to give compound **1** in 61% yield. Montmorillonite K 10 Clay in MeOH/water 1:1 was used for slightly acidic conditions. This reagent also cleaves acetals and 4,4′-dimethoxytrityl protecting groups.[28] Compounds **1i** and **1** were treated with K 10 Clay in MeOH/H_2O at 150 °C for 4 min and 3 min, respectively, to give glucose in high yields (85% and 91%, respectively). This can be compared to the original conditions (75 °C for 72 h, 77% yield) for deprotection of compound **1** to glucose.[29] Similarily, compound **4** was treated with K 10 Clay in MeOH/H_2O for 2 min at 150 °C to give compound **4b** in 89% yield. Since polymer supported reagents worked out well for the acylation reaction, we treated compound **3c** with polymer supported PPTS (poly(4-vinylpyridinium *p*-toluenesulfonate)) in EtOH/H_2O at 150 °C for 2 min to give methyl α-D-glucopyranoside (**3**) in 94% yield.

CONCLUSIONS

Microwave-heating has been shown to be a most useful method to assist protecting group manipulation reactions on saccharides. Short reaction times and large rate enhancements as compared to conventional methods are observed, notably in reactions using mild reagents or involving steric hindrance. Yields are comparable or better than when using conventional methods, and sometimes much higher in reactions where the short reaction time prevents decomposition. The short reaction times in combination with the easy performance and work-up, especially when using solid-supported reagents, make the method most attractive and also suitable for automation.

EXPERIMENTAL

General Methods. The microwave assisted reactions were performed in a Smithsynthesizer, a single mode microwave cavity, from Personal Chemistry. NMR spectra were recorded in $CDCl_3$ with Me_4Si as internal standard at 25 °C, using a Varian Mercury 300 instrument at 300 MHz (^1H)/75 MHz (^{13}C). All NMR spectra recorded were in agreement with the postulated structures and only selected data are reported. TLC was performed on silica gel 60 F_{254} (Merck) and the products were detected by visualization under 254 nm light and charring with 8% H_2SO_4 (aq). The samples were purified by flash chromatography on Silica Gel (0.0404–0.063 mm, Amicon) eluted with toluene/EtOAc 4:1–1:1, unless otherwise stated. Optical rotations were recorded at room temperature with a Perkin-Elmer 241 polarimeter using a 10 cm, 1 mL cell. All starting reagents were of the best grade available (Aldrich or Lancaster) and were used without purification. The

solid supported reagents were from Argonaut technologies or Aldrich. **CAUTION: These reactions are not recommended to be carried out in a multimode domestic microwave oven due to nonuniform irradiation and no temperature control (risk of explosion and thermal runaway)**. Also observe that the reactions are run in a closed vessel (screwcap with a septum) and that in several cases the pressure during the reaction is between 5–10 bar.

3-*O*-Acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1a). *Method A*: 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) (100 mg, 0.38 mmol) was dissolved in MeCN (2 mL). Acetyl chloride (55 μL, 0.77 mmol) and pyridine (93 μL, 1.15 mmol) were added to the solution. The sample was irradiated for 12 min at 170 °C. The mixture was diluted with MeOH, concentrated and purified to give **1a** (93 mg, 0.31 mmol, 80%).

Method B: To a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL), acetyl chloride (55 μL, 0.77 mmol) and *N,N*-(diisopropyl)aminoethylpolystyrene (PS-DIEA) (300 mg, 1.15 mmol) were added. The sample was irradiated for 20 min at 165 °C. The mixture was then filtered, concentrated and purified to give **1a** (77 mg, 0.25 mmol, 66%).

Method C: To a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL), acetyl chloride (83 μL, 1.15 mmol) and *N*-(methylpolystyrene)-4-(methylamino)pyridine (PS-DMAP) (402 mg, 1.54 mmol) were added. The sample was irradiated for 15 min at 180 °C and worked up and purified as described for Method B to give **1a** (99 mg, 0.32 mmol, 85%). **1a**: $[\alpha]_D$ −33° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −31°).[10]

3-*O*-Chloroacetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1b). To compound **1** (100 mg, 0.38 mmol) in MeCN (2 mL), chloroacetyl chloride (60 αL, 0.77 mmol) and pyridine (60 μL, 0.77 mmol) were added. Irradiation of the sample was performed for 8 min at 100 °C. The mixture was diluted with MeOH, concentrated and purified to give **1b** (123 mg, 0.36 mmol, 95%): $[\alpha]_D$ −32° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −33°).[31]

3-*O*-Pivaloyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1c) and 6-*O*-Pivaloyl-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (2c). *Method A*: Pivaloyl chloride (95 μL, 0.77 mmol) and pyridine (93 μL, 1.15 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL). The sample was irradiated for 15 min at 170° C. The mixture was diluted with MeOH, concentrated and purified to give **1c**+**2c** (3:1, 112 mg, 0.32 mmol, 85%).

Method B: Pivaloyl chloride (95 μL, 0.77 mmol) and PS-DIEA (300 mg, 1.15 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL). The sample was irradiated for 20 min at 160 °C. The mixture was filtered, concentrated and purified to give **1c** (105 mg, 0.30 mmol, 79%).

Method C: Pivaloyl chloride (141 μL, 1,15 mmol) and PS-DMAP (402 mg, 1.54 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL). The sample was irradiated for 15 min at 180 °C. The mixture was filtered, concentrated and purified to give **1c** (116 mg, 0.34 mmol, 88%). **1c**: $[\alpha]_D$ −26° (*c* 1.0,

$CHCl_3$). ^{13}C NMR ($CDCl_3$) δ 67.9 (C-6), 72.6, 76.0, 80.5, 83.5 (C-2,-5), 105.33 (C-1), 109.4, 112.4 ($(CH_3)_2COO$), 176.9 (COO, ester). (lit. ref. ^{13}C NMR ($CDCl_3$) δ 105.2 (C1), 109.2, 112.2 ($(CH_3)_2COO$), 176.6 (COO, ester).[9]

3-*O*-Benzoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1d) and 6-*O*-Benzoyl-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (2d). *Method A*: Compound **1** (100 mg, 0.38 mmol) was dissolved in MeCN (2 mL). Benzoyl chloride (89 μL, 0.77 mmol) and pyridine (124 μL, 1.54 mmol) were added to the solution. The sample was irradiated for 10 min at 170 °C. The mixture was diluted with MeOH, concentrated and purified to give **1d**+**2d** (3:1, 134 mg, 0.37 mmol, 95%).

Method C: Benzoyl chloride (89 μL, 0.77 mmol) and PS-DMAP (1040 mg, 1.54 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL). The sample was irradiated for 15 min at 170 °C. The mixture was filtered, concentrated and purified to give **1d** (124 mg, 0.34 mmol, 89%). **1d**: $[\alpha]_D$ −50° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −49.7°, EtOH).[10]

3-*O*-Allyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1e). Allyl bromide (49 μL, 0.58 mmol) and sodium hydride (23 mg, 0.58 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL). Irradiation of the sample was performed for 1 min at 190 °C. The mixture was diluted with MeOH, concentrated and purified to give **1e** (101 mg, 0.33 mmol, 88%): $[\alpha]_D$ −24° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −28.8°).[32]

3-*O*-Benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1f). *Method A*: Compound **1** (100 mg, 0.38 mmol) was dissolved in MeCN (2 mL) and benzyl chloride (133 μL, 1.15 mmol) and potassium hydroxide (107 mg, 1.92 mmol) were added to the solution. The sample was irradiated for 2 min at 150 °C. Purification gave **1f** (132 mg, 0.38 mmol, 98%).

Method B: To a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL), benzyl chloride (66 μL, 0.58 mmol) and sodium hydride (23 mg, 0.58 mmol) were added. The sample was irradiated for 1 min at 190 °C. Methanol was added to quench the reaction. Purification gave **1f** (128 mg, 0.36 mmol, 95%).

Method C: Benzyl bromide (114 μL, 0.96 mmol) and silver oxide (89 mg, 1.15 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL). The sample was irradiated for 20 min at 190 °C. The mixture was diluted with MeOH, filtered, concentrated and purified to give **1f** (91 mg, 0.26 mmol, 68%).

Method D: To a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL), benzyl bromide (69 μL, 0.58 mmol) and sodium hydride (23 mg, 0.58 mmol) were added. Irradiation of the sample was performed for 1 min at 180 °C. The mixture was diluted with MeOH, concentrated and purified to give **1f** (129 mg, 0.37 mmol, 96%). **1f**: $[\alpha]_D$ −26° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −26.4°).[13]

3-*O*-*p*-Methoxybenzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1g). Compound **1** (100 mg, 0.38 mmol) was dissolved in MeCN (2 mL). *p*-

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Methoxybenzyl chloride (130 μL, 0.96 mmol) and potassium hydroxide (64 mg, 1.15 mmol) were added to the solution. The sample was irradiated for 5 min at 160 °C. Purification gave **1g** (132 mg, 0.35 mmol, 90%): $[\alpha]_D$ −27° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −17°).[33]

3-*O*-*o*-Nitrobenzyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1h). *o*-Nitrobenzyl bromide (166 mg, 0.77 mmol) and sodium hydride (31 mg, 0.77 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in MeCN (2 mL). The sample was irradiated for 2 min at 180 °C. The mixture was quenched with MeOH, concentrated and purified to give **1h** (143 mg, 0.36 mmol, 94%): $[\alpha]_D$−38° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.33, 1.34, 1.43, 1.51 (s, 12H, CH_3), 4.00–4.03 (m, 1H, H-6), 4.10–4.17 (m, 3H, H-3, H-4, H-6), 4.33–4.40 (m, 1H, H-5), 4.66–4.68 (d, 1H, H-2), 4.98–5.03 (d, 1H, CH_2 benzyl), 5.12–5.17 (d, 1H, CH_2 benzyl), 5.92–5.93 (d, 1H, $J_{1,2}$ = 3.57 Hz, H-1), 7.43–8.10 (m, 4H, aromatic H); ^{13}C NMR ($CDCl_3$) δ 25.6, 26.5, 27.1 (CH_3), 67.8 (C-6), 68.9 (C-5), 72.5 (CH_2-Bn), 81.4 (C-4), 82.4 (C-3), 82.6 (C-2), 105.4 (C-1), 109.3, 112.1 ((CH_3)$_2$COO), 124.8, 128.3, 128.9, 133.8, 134.5 147.2 (aromatic C).

Anal. Calcd for $C_{19}H_{25}NO_8$ (395.40): C, 57.71; H, 6.37; N, 3.54. Found: C, 57.92; H, 6.28; N; 3.69.

3-*O*-*tert*-Butyldimethylsilyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1i) and 6-*O*-*tert*-Butyldimethylsilyl-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose (2i). *Method A: tert*-Butyldimethylsilyl chloride (116 mg, 0.77 mmol) and imidazole (52 mg, 0.77 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in DMF (2 mL). The sample was irradiated for 10 min at 200 °C. The mixture was diluted with toluene and extracted with water. The organic layer was dried ($MgSO_4$), filtered and concentrated. Purification gave **1i**+**2i** (3:1, 136 mg, 0.36 mmol, 94%).

Method B: tert-Butyldimethyl silyl chloride (116 mg, 0.77 mmol) and PS-DMAP (780 mg, 1.15 mmol) were added to a solution of **1** (100 mg, 0.38 mmol) in DMF (2 mL). The sample was irradiated for 15 min at 180 °C. The mixture was filtered, concentrated and purified to give **1i**+**2i** (3:1, 120 mg, 0.32 mmol, 83%).

3-*O*-Trimethylsilyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1j). *N,O*-Bis-(trimethylsilyl)acetamide (BSA) (285 μL, 1.15 mmol) was added to a solution of **1** (100 mg, 0.38 mmol) in DMF (2 mL). The sample was irradiated for 15 min at 190 °C. The mixture was worked up as described above in method A. Purification gave **1j** (119 mg, 0.36 mmol, 93%). $[\alpha]_D$ −18° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −16.9°).[34]

Methyl 2,3,4,6-Tetra-*O*-pivaloyl-α-D-glucopyranoside (3a). To a solution of methyl α-D-glucopyranoside (**3**) (100 mg, 0.51 mmol) in MeCN (2 mL), pivaloyl chloride (282 μL, 2.31 mmol) and pyridine (248 μL, 3.07 mmol) were added. The sample was irradiated for 10 min at 160 °C, whereafter the mixture was

diluted with MeOH, concentrated and purified to give **3a** (185 mg, 0.35 mmol, 68%): $[\alpha]_D$ +105° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ +102°).[11]

Methyl 2,3,4,6-Tetra-*O*-trimethylsilyl-α-D-glucopyranoside (3b). To a solution of **3** (100 mg, 0.51 mmol) in DMF (2 mL), BSA (1018 μL, 4.12 mmol) was added. The sample was irradiated for 10 min at 180 °C. Purification gave **3b** (89 mg, 0.27 mmol, 70%): $[\alpha]_D$ +80° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ +79.7°).[35]

Methyl 4,6-*O*-Benzylidene-α-D-glucopyranoside (3c). Benzal bromide (166 μL, 1.0 mmol) and PS-DMAP (1044 mg, 1.54 mmol) were added to a solution of compound **2** (100 mg, 0.51 mmol) in MeCN (2 mL). The sample was irradiated for 5 min at 170° C. Purification gave **3c** (121 mg, 0.43 mmol, 83%): $[\alpha]_D$ +89° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ +105°).[36]

Ethyl 4,6-*O*-Benzylidene-1-thio-β-D-glucopyranoside (4a). Ethyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**4**) (100 mg, 0.19 mmol) was treated with Et_3N/MeOH/H_2O 1:5:1 (2 mL) and irradiated at 150 °C for 15 min,. The mixture was concentrated and purified (toluene/EtOAc 1:1) to give **4a** (47 mg, 0.15 mmol, 78%): $[\alpha]_D$ −61° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$ −65°).[37]

Ethyl 2,3-Di-*O*-benzoyl-1-thio-β-D-glucopyranoside (4b). Compound **4** (50 mg, 0.10 mmol) was treated with Montmorillonite K 10 Clay (50 mg) in MeOH/H_2O 1:1 (2 mL) and irradiated for 2 min at 150° C. The mixture was filtered, concentrated and purified (toluene/EtOAc 1:1) to give **4b** (37 mg, 0.08 mmol, 89%): $[\alpha]_D$ +63° (*c* 1.0, $CHCl_3$). (lit. ref. $[\alpha]_D$+87.6°).[38]

Deacylation of 3-*O*-Benzoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1d). Compound **1d** (55 mg, 0.15 mmol) was treated with Et_3N/MeOH/H_2O 1:5:1 (2 mL), and irradiated for 15 min at 150 °C or with KCN (10 mg, 0.15 mmol) in 2 mL EtOH/H_2O 1:1 and irradiated for 3 min at 120 °C. The mixtures were concentrated and purified to give compound **1** (28 mg, 0.11 mmol, 71%), respectively, (26 mg, 0.10 mmol, 67%).

Desilylation of 3-*O*-*tert*-Butyldimethylsilyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1i). To a solution of **1i** (55 mg, 0.147 mmol) in MeCN (2 mL), Bu_4NBr (95 mg, 0.29 mmol), potassium fluoride (17 mg, 0.29 mmol) and H_2O (0.1 mL) were added. The sample was irradiated for 2 min at 180 °C. Purification (toluene/EtOAc 1:1) gave **1** (23 mg, 0.09 mmol, 61%).

Deprotection of 1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (1) and 3-*O*-*tert*-Butyldimethylsilyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1i). Compound **1** (100 mg, 0.38 mmol) and compound **1i** (100 mg, 0.26 mmol) were treated with Montmorillonite K 10 Clay (200 mg) in MeOH/H_2O 1:1 (2 mL) and irradiated for 3 and 4 min, respectively, at 150° C. The mixtures were filtered, concentrated and purified (EtOAc:H_2O: EtOH:AcOH; 20:3:3:2) to give glucose

from compound **1** (63 mg, 0.35 mmol, 91%) and from compound **1i** (40 mg, 0.22 mmol, 85%).

Deacetalation of Methyl 4,6-*O*-Benzylidene-α-D-glucopyranoside (3c). Compound **3c** (100 mg, 0.35 mmol) was treated with poly-4-vinylpyridinium *p*-toluenesulfonate (200 mg) in EtOH/H_2O 1:1 (2 mL) at 150 °C for 2 min. The mixture was filtered, concentrated and purified (EtOAc:H_2O:EtOH:AcOH; 20:3:3:2) to give compound **3** (64 mg, 0.33 mmol, 94%).

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