Supporting Information

Organosilicon-mediated Regioselective Acetylation of Carbohydrates

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Contents

General: All commercially available starting materials and solvents were of reagent grade and used without further purification. Chemical reactions were monitored with thin-layer chromatography using precoated silica gel 60 (0.25 mm thickness) plates. Flash column chromatography was performed on silica gel 60 (SDS 0.040-0.063 mm). ^{1}H NMR spectra were recorded at 298K in $CDCl_3$, using the residual signals from $CHCl_3$ (^{1}H: δ = 7.25 ppm) as internal standard. ^{1}H peak assignments were made by first order analysis of the spectra, supported by standard ^{1}H-^{1}H correlation spectroscopy (COSY).

General method for organosilicon-mediated regioselective acylation: The 1,2- or 1,3-diol reactants (100 mg) were allowed to react with dimethyl dimethoxysilane (2.0 eq.) or methyl trimethoxysilane (1.2 eq.) in acetonitrile (10 mL) at 80 ^{o}C for 5 hours. After removal of most of the solvent, the residues were allowed to react with acetic anhydride or acetic chloride (1.1 eq.) in dry acetonitrile (1 mL) at 40 ^{o}C for 6-12 hours in the presence of tetrabutylammonium acetate (0.3 eq.). The reaction mixture was directly purified by flash column chromatography on silica gel (eluent: hexanes/EtOAc = 5:1 to 1:2), affording the pure selectively protected derivatives.

General method for obtaining product ratios: The 1,2- or 1,3-diol reactants (50 mg) were allowed to react with methyl trimethoxysilane (1.2 eq.) in acetonitrile (10 mL) at 80 ^{o}C for 5 hours. After removal of most of the solvent, the residues were allowed to react with acetic anhydride (1.1 eq.) in dry acetonitrile (1 mL) at 40 ^{o}C for 6 hours in the presence of tetrabutylammonium acetate (0.3 eq.). Samples of the reaction mixtures (0.2 mL) were withdrawn, dried under vacuum, and the product distribution analyzed using ^{1}H-NMR spectroscopy.

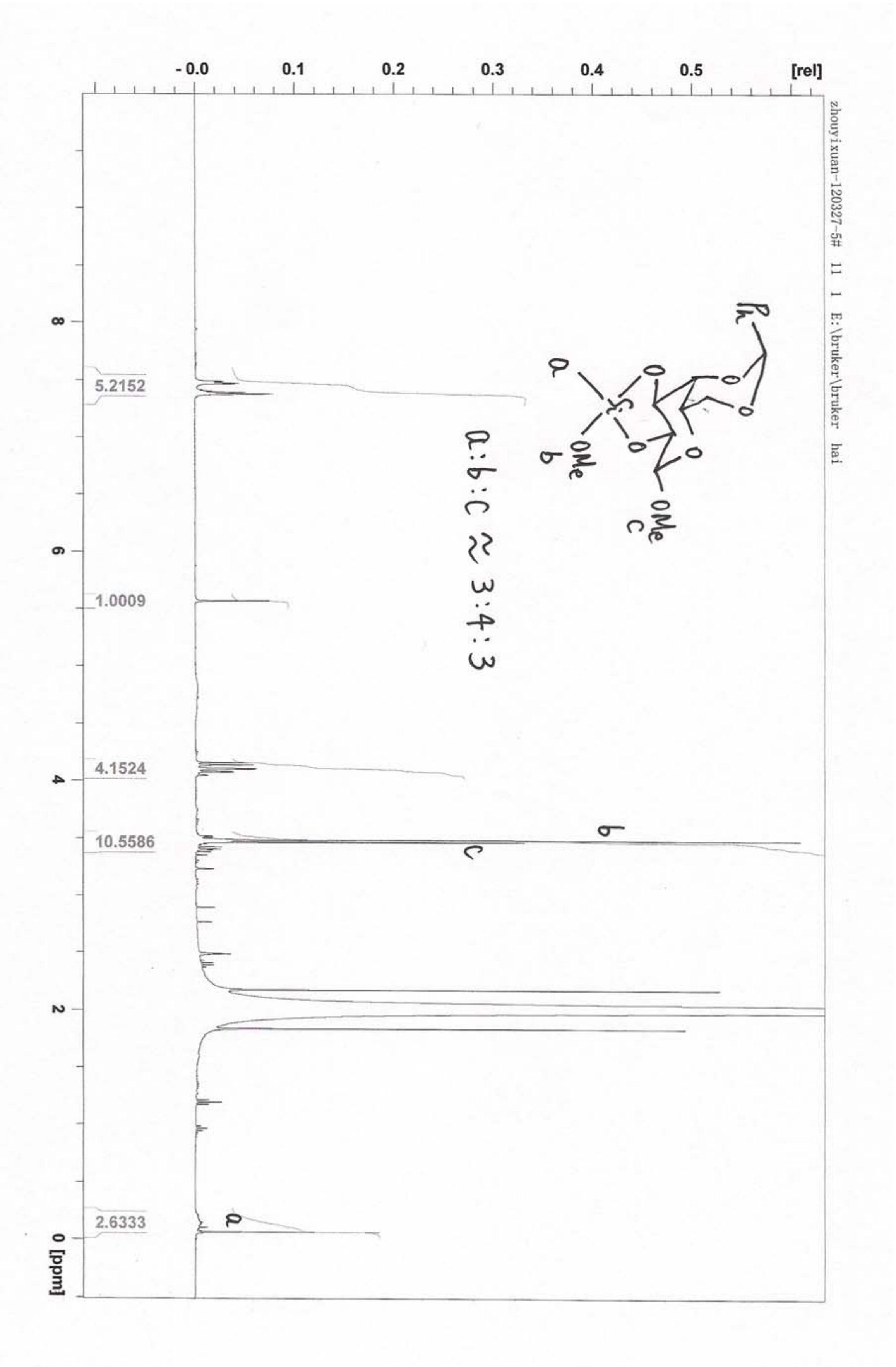


Figure S1. ^{1}H-NMR analysis of the formation of the dioxasilolane intermediate for 4,6-*O*-benzylidene-β-D-galactoside **1.** The ratio of a:b decreased from 3:9 for methyl trimethoxysilane into 3:4. (The value of 10.56 includes 6 H from compound **1** and 4 H from SiOMe).

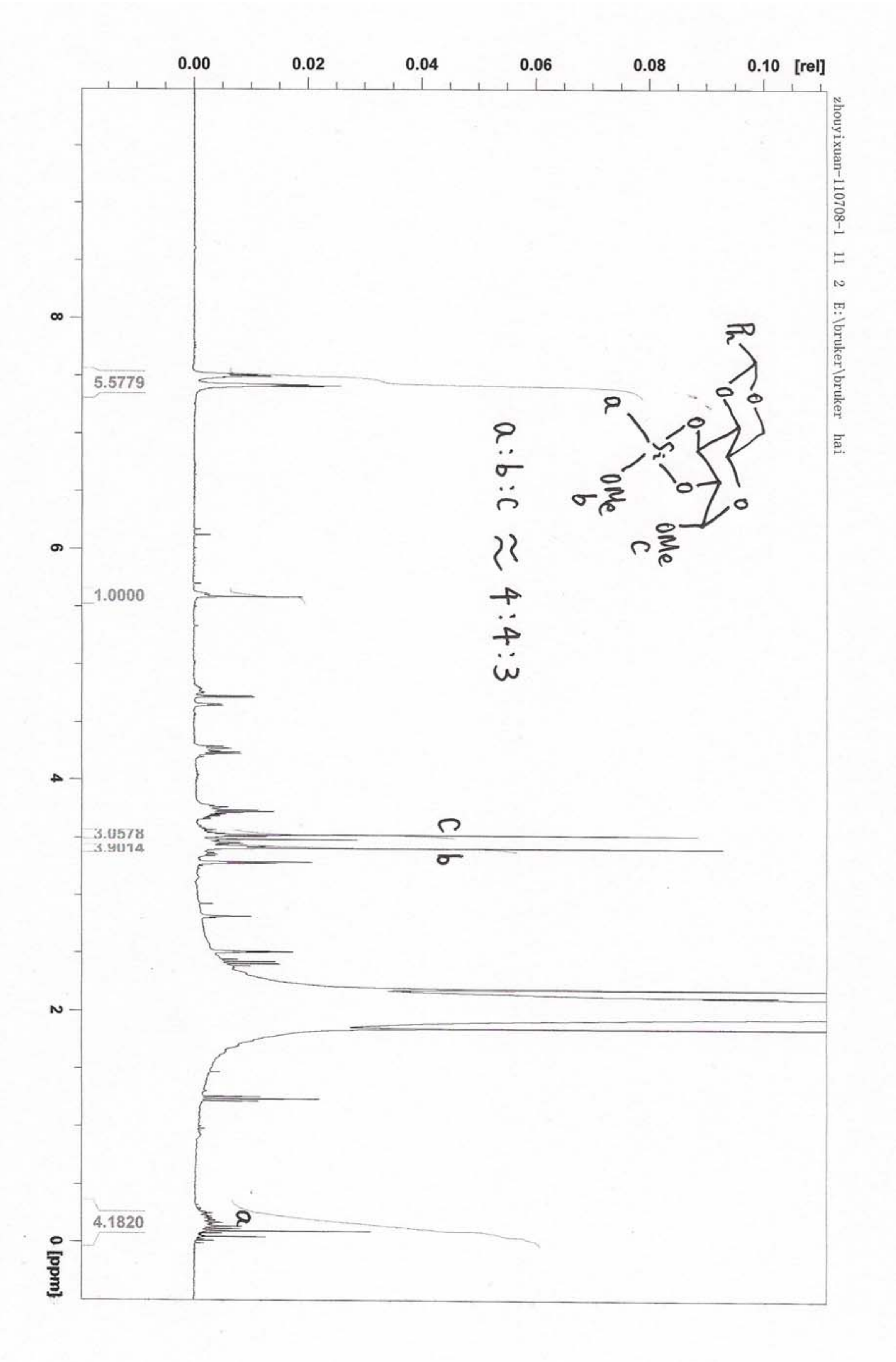
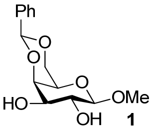
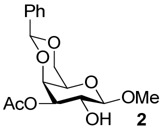
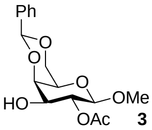
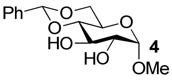
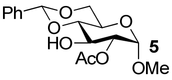
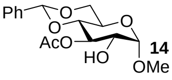
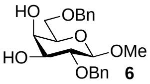
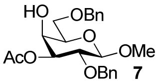
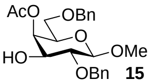
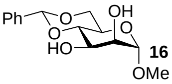
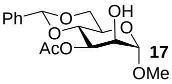
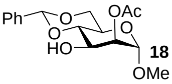
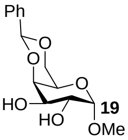
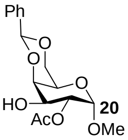
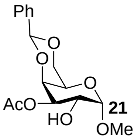
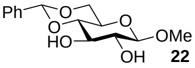
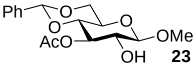
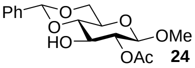
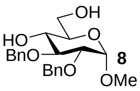
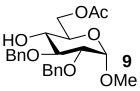
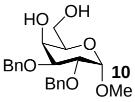
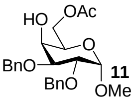
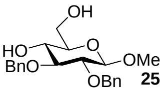
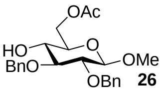
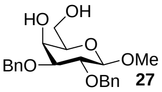
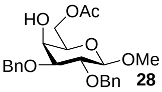
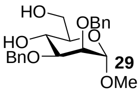
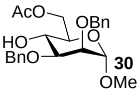
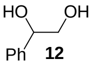
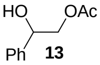
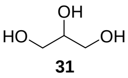
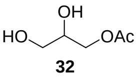
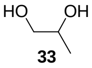
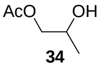


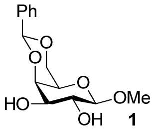
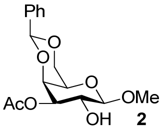
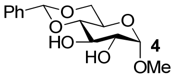
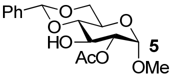
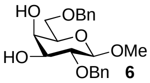
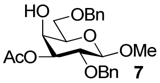
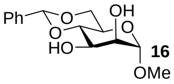
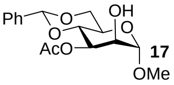
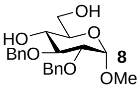
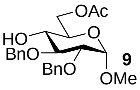
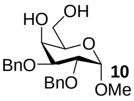
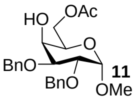
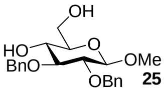
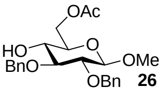
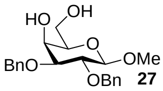
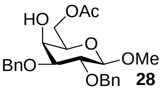
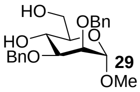
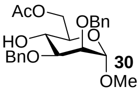
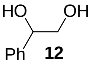
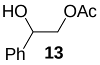
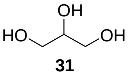
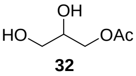
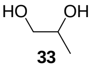
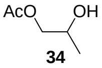
Figure S2. ^{1}H-NMR analysis of the formation of the dioxasilolane intermediate for 4,6-*O*-benzylidene-α-D-glucoside **4.** The ratio of a:b decreased from 3:9 for methyl trimethoxysilane into 4:4.

Table S1. Product distribution in organosilicon-mediated acetylation of 1,2- and 1,3-diols.[a]

Entry	Reactant	Major product	Minor product	NMR ratio
1	 **1**	 **2**	 **3**	76/24
2	 **4**	 **5**	 **14**	67/33
3	 **6**	 **7**	 **15**	80/20
4	 **16**	 **17**	 **18**	73/27
5	 **19**	 **20**	 **21**	57/43
6	 **22**	 **23**	 **24**	56/44
7	 **8**	 **9**	-	>93
8	 **10**	 **11**	-	>96
9	 **25**	 **26**	-	>94
10	 **27**	 **28**	-	>92
11	 **29**	 **30**	-	>91
12	 **12**	 **13**	-	>90
13	 **31**	 **32**	-	>95
14	 **33**	 **34**	-	>90

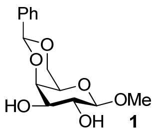
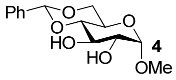
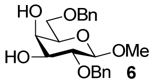
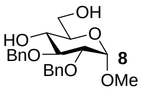
[a] Reaction conditions: reactant (50 mg), TBAOAc (0.3 eq.), $MeSi(OMe)_3$ (1.2 eq.) and Ac_2O (1.1 eq.), 40 °C, 6h.

Table S2. Isolated yields in organosilicon/organotin-mediated acylation.

Entry	Reactant	Major product	Yields (organosilicon)	Yields (organotin)
1	 **1**	 **2**	74	72[1]
2[a]	 **4**	 **5**	63	72[2]
3	 **6**	 **7**	79	85[3]
4[a]	 **16**	 **17**	61	67[4]
5[b]	 **8**	 **9**	80	79-90[5]
6	 **10**	 **11**	84	85
7[b]	 **25**	 **26**	86	79-90[5]
8	 **27**	 **28**	81	85
9[b]	 **29**	 **30**	82	79-90[5]
10[c]	 **12**	 **13**	85	70-84[6]
11[c]	 **31**	 **32**	73	70-84[6]
12[c]	 **33**	 **34**	73	70-84[6]

[a] Benzoyl chloride as acylation reagent; organotin method. [b] Similar 1,3-diol configuration; slightly different substrate; benzoyl chloride as acylation reagent; organotin method. [c] Similar 1,2-diol configuration, slightly different substrate.

Table S3. Product distribution in acylation using acetyl chloride/ triethylamine.[a]

Substrate	Starting material	2-OAc	3-OAc	4-OAc	6-OAc	di-OAc
 1	0.8	0.07	0.13			
 4	0.16	0.4	0.4			0.04
 6	0.68		0.17	0.15		
 8	0.36				0.64	

[a] Reaction conditions: Substrate (1 eq.), AcCl (1 eq.), DCM, TEA (2 eq.), 0 °C, 24 h.

^{1}H-NMR data

Methyl 3-*O*-acetyl-4,6-*O*-benzylidene-β-D-galactopyranoside (2)[7]

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.48-7.38 (aromatic protons), 5.50 (1H, s, PhCH), 4.86 (1H, dd, J = 3.5, 10.0 Hz, H_3), 4.40 (1H, dd, J = 1.0, 3.5 Hz, H_6), 4.34 (1H, dd, J = 1.5, 12.5 Hz, H_6), 4.29 (1H, d, J = 7.5 Hz, H_1), 4.07 (1H, dd, J = 1.5, 7.5 Hz, H_4), 4.01 (1H, dd, J = 7.5, 10.0 Hz, H_2), 3.59 (3H, s, OCH_3), 3.51 (1H, d, J = 1.5 Hz, H_5), 2.43 (1H, br, OH), 2.14 (3H, s, OAc).

Methyl 2-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside (5)[8]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.50-7.30 (aromatic protons), 5.53 (1H, s, PhCH), 4.93 (1H, d, J = 3.6 Hz, H_1), 4.78 (1H, t, J = 9.6 Hz, H_2), 4.28 (1H, dd, J = 4.0, 10.0 Hz, H_6), 4.15 (1H, t, J = 10.0 Hz, H_3), 3.85 (1H, td, J = 10.0, 10.0 Hz, H_5), 3.74 (1H, t, H_6), 3.53 (1H, t, H_4), 3.39 (3H, s, OCH_3), 2.14 (3H, s, OAc).

Methyl 3-*O*-acetyl-2,6-di-*O*-benzyl-β-D-galactopyranoside (7)[9]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.26-7.36 (10H, m, 2xOBn), 4.88, 4.60, 4.59, 4.56 (4H, d, $J_{a,b}$ = 12.1 Hz, $2xOCH_aH_bC_6H_5$), 4.35 (1H, d, J = 7.9 Hz, H_1), 3.76 (2H, dd, J = 4.6, 3.0 Hz, $2xH_6$), 3.61 (1H, td, J = 9.3, 3.8 Hz, H_4), 3.56 (3H, s, OCH_3), 3.46-3.51 (1H, m, H_5), 3.33 (1H, dd, J = 7.9, 9.3 Hz, H_2), 2.92 (1H, d, J = 3.8 Hz, OH), 2.00 (3H, s, OAc).

Methyl 2,3-di-*O*-benzyl-6-*O*-acetyl-α-D-glucopyranoside (9)[10]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.46-7.26 (10H, m, 2xOBn), 5.00 (1H, d, *J* = 11.2 Hz, $OCH_2C_6H_5$), 4.78 (1H, d, *J* = 12.2 Hz, $OCH_2C_6H_5$), 4.75 (1H, d, *J* = 11.2 Hz, $OCH_2C_6H_5$), 4.65 (1H, d, *J* = 12.2 Hz, $OCH_2C_6H_5$), 4.62 (1H, d, *J* = 3.6 Hz, H_1), 4.41 (1H, dd, *J* = 12.2, 4.6 Hz, H_6), 4.21 (1H, dd, *J* = 12.2, 1.8 Hz, $H_{6'}$), 3.79 (1H, merged dd, *J* = 9.3, 9.0 Hz, H_3), 3.76-3.72 (1H, m, H_5), 3.50 (1H, dd, *J* = 9.5, 3.6 Hz, H_2), 3.44-3.39 (1H, m, H_4), 3.38 (3H, s, OCH_3), 2.47 (1H, bs, OH), 2.08 (3H, s, OAc).

Methyl 2,3-di-*O*-benzyl-6-*O*-acetyl-α-D-galactopyranoside (11)[11]

^{1}H-NMR (DMSO, 400 MHz): δ 7.41-7.27 (10H, m, $2xOCH_2C_6H_5$), 4.96 (1H, d, *J* = 4.8 Hz, 4-OH), 4.79 (1H, d, *J* = 3.6 Hz, H_1), 4.72-4.56 (4H, m, $2xOCH_2C_6H_5$), 4.15-4.11 (2H, m, $2xH_6$), 4.05 (1H, t, H_4), 3.80-3.74 (2H, m, H_2, H_5), 3.69-3.65 (1H, dd, *J* = 10.4, 3.0 Hz, H_3), 3.26 (3H, s, OCH_3), 2.02 (3H, s, OAc).

3,4-Dihydroxy-4-phenylbutan-2-one (13)[12]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.42-7.28 (aromatic protons), 4.98-4.95 (1H, dd, *J* = 8.4, 3.2 Hz, CH), 4.32-4.15 (2H, m, CH_2), 2.12 (3H, s, OAc).

Methyl 3-*O*-acetyl-4,6-*O*-benzylidene-α-D-mannopyranoside (17)[13]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.46–7.26 (aromatic protons), 5.55 (1H, s, PhCH), 5.32 (1H, dd, *J* = 10.1, 3.3 Hz, H_3), 4.75 (1H, d, *J* = 1.5 Hz, H_1), 4.30 (1H, dd, *J* = 10.1, 4.2 Hz, H_6), 4.15 (1H, dd, *J* = 3.3, 1.5 Hz, H_2), 4.09 (1H, dd, *J* = 10.1, 10.1 Hz, H_6), 3.93 (1H, m, H_5), 3.84 (1H, dd, *J* = 10.1, 10.1 Hz, H_4), 3.40 (3H, s, OCH_3), 2.13 (3H, s, OAc).

Methyl 2-*O*-acetyl-4,6-*O*-benzylidene-α-D-galactopyranoside (20)[7]

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.50-7.37 (aromatic protons), 5.57 (1H, s, PhCH), 5.16 (1H, dd, *J* = 3.6, 10.2 Hz, H_2), 4.98 (1H, d, *J* = 3.6 Hz, H_1), 4.28-4.32 (2H, m, H_6, H_5), 4.07-4.12 (2H, m, H_4, H_6), 3.74 (d, 1H, *J* = 10.5 Hz, H_3), 3.40 (3H, s, OCH_3), 2.40 (1H, br, OH), 2.15 (3H, s, OAc).

Methyl 3-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranoside (23)[14]

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 5.50 (lH, s, PhCH), 5.21 (lH, t, *J* = 9.3 Hz, H_3), 4.38 (lH, d, *J* = 8.7 Hz, H_1), 4.36 (lH, dd, *J* = 10.5, 5.4 Hz, H_6), 3.78 (lH, t, 10.5 Hz, H_6), 3.63 (1H, t, *J* = 9.8 Hz, H_4), 3.58 (3H, s, OCH_3), 2.13 (3H, s, OAc).

Methyl 2,3-di-*O*-benzyl-6-*O*-acetyl-β-D-glucopyranoside (26)[15]

^{1}H-NMR (DMSO, 400 MHz): δ 7.35-7.25 (10H, m, 2x$OCH_2C_6H_5$), 5.54 (1H, d, *J* = 6.0 Hz, 4-OH), 4.37 (1H, d, *J* = 8.0 Hz, H_1), 4.85-4.62 (4H, m, 2x$OCH_2C_6H_5$), 4.30-4.27 (1H, dd, *J* = 12.0, 1.6 Hz , H_6), 4.14-4.10 (1H, dd, *J* = 12.0, 6.2 Hz, H_6), 3.47-3.34 (3H, m, H_3, H_4, H_5), 3.44 (3H, s, OCH_3), 2.05 (3H, s, OAc).

Methyl 2,3-di-*O*-benzyl-6-*O*-acetyl-β-D-galactopyranoside (28)[11]

^{1}H-NMR (DMSO, 400 MHz): δ 7.39-7.25 (10H, m, 2x$OCH_2C_6H_5$), 4.75 (1H, d, *J* = 5.6 Hz, 4-OH), 4.76-4.51 (4H, m, 2x$OCH_2C_6H_5$), 4.28 (1H, d, *J* = 7.6 Hz, H_1), 4.22-4.13 (2H, m, H_{6a}, H_{6b}), 3.97 (1H, t, H_4), 3.66 (1H, t, H_5), 3.49 (2H, s, H_2, H_3), 3.48 (3H, s, OCH_3), 2.04 (3H, s, OAc).

Methyl 6-*O*-acetyl-2,3-di-*O*-benzyl-α-D-mannopyranoside (30)[16]

^{1}H-NMR (DMSO, 400 MHz): δ 7.39-7.28 (10H, m, 2x$OCH_2C_6H_5$), 5.32 (1H, d, *J* = 6.0 Hz, 4-OH), 4.77 (1H, d, *J* = 0.8 Hz, H_1), 4.65-4.62 (4H, m, 2x$OCH_2C_6H_5$), 4.35-4.31 (1H, dd, *J* = 12.0, 1.8 Hz, H_6), 4.10-4.03 (1H, m, H_6), 3.81 (1H, t, H_2), 3.69-3.61 (1H, m, H_4), 3.66-3.51 (2H, m, H_3, H_5), 3.26 (3H, s, OCH_3), 2.02 (3H, s, OAc).

2,3-Dihydroxypropyl acetate (32)[17]

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 4.20-4.10 (2H, m), 3.93 (1H, t, *J* = 4.8 Hz), 3.69 (1H, dd, *J* = 3.6, 11.6 Hz), 3.59 (1H, dd, *J* = 6.0, 11.6 Hz), 3.19-3.09 (1H, bs, OH), 2.80-2.70 (1H, bs, OH), 2.11 (3H, s, Oac).

2-hydroxypropyl acetate (34)[18]

^{1}H-NMR (DMSO, 400 MHz): δ 3.60 (1H, m, CH), 3.30–3.12 (2H, m, CH_2), 2.00 (3H, s, Oac), 1.18 (3H, d, *J* = 6.3 Hz, CH_3).

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