DOI: 10.1002/ejoc.201101708

Hydroxy Group Acidities of Partially Protected Glycopyranosides

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Keywords: Carbohydrates / Glycosides / Acidity / Hydrogen bonds / Reactivity

A comprehensive acidity study of carbohydrate hydroxy groups has been carried out. Relative acidities (K_e) were determined spectrophotometrically for partially methylated methyl α-D-glycopyranosides. Apparently, the acidity is strongly affected by intramolecular hydrogen bonding as well as stereochemistry and solvation. By comparison with pK_e and pK_a values of aliphatic alcohols and polyols the first estimation of the pK_a values for partially protected glycopyranosides was obtained. These findings contribute to the understanding of the relative reactivities of carbohydrate hydroxy groups.

Introduction

The polyhydroxyl nature of carbohydrates complicates their selective functionalization, particularly glycosylation reactions, which are the key process in the chemical synthesis of complex oligosaccharides of biological relevance. Carbohydrate hydroxy groups do not only show similar reactivities, which give rise to regioisomer problems, but also often exhibit anomalous reactivities that lead to unusual, often undesired results. To date, the most reliable method for selective glycosylation is the implementation of extended protecting group chemistry or the use of enzymes that activate one particular hydroxy group. However, both approaches have drawbacks, namely, multistep synthesis in the former and restriction to specific substrates in the latter.[1]

With the aim to decrease the number of tedious protection and deprotection transformations, studies towards chemical "enzyme-like" glycosylation with ubiquitous applications require essentially systematic determination and control of individual hydroxy group reactivities.

Previously, there have been proposals to deal with the relative reactivities of carbohydrate hydroxy groups.[2] Intramolecular hydrogen bonding is assumed to play a significant role in the differentiation of hydroxy group reactivities and the acidity of carbohydrates of partially protected or unprotected sugar derivatives.[3–5] Even though some are difficult to understand,[6,7] as a major finding hydrogen bond networks are apparently responsible for the differences in regioselectivity towards acylating and alkylating reagents.[8–10]

The enhanced reactivities of particular hydroxy groups by prior base activation of partially protected acceptors have been revealed and lead to high selectivities.[11,12]

Considering the mechanism of base-promoted glycosylation, the observed outcome strongly suggests intramolecular hydrogen bonding.

As a contribution to a more profound understanding of carbohydrate hydroxy reactivities of partially protected monosaccharides it was considered worthwhile to attempt the determination of the acidic properties of partially protected sugar derivatives. The results obtained could explain selective synthesis or partial substitution. Additionally, it could be elucidated whether and to what extent hydrogen bonding affects the acidity.

The first report of dissociation constants of carbohydrates concerned aldohexoses, hexopyranosides and alditols.[13] Two major findings were obtained: aldohexoses are more acidic than the corresponding alditols and methyl glycopyranosides, respectively, which is explained by the absence of the hemiacetal group in alditols. The pK value of D-glucose was 12.2, 13.6 for sorbitol and 13.6 and 13.7 for methyl β- and α-glucopyranoside, respectively. Furthermore, the acidity of polyols increases with the number of hydroxy groups, however, this observation was unexplained. Later studies have been restricted to aldohexoses and alditols and have also employed semiempirical calculations.[4,14,15]

The pK_a values of aminodeoxyglycosides as a model system have been determined by Bols and coworkers.[16] The amino pK_a values as electron density measurements correlated with the nucleophilicity of the corresponding hydroxy group at these positions and quantified their reactivity. The authors established the pK_a scale 4-NH_2 > 2-NH_2 > 3-NH_2 > 6-NH_2 and observed that the stereochemistry and

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201101708 or from the author.

anomeric configuration influenced the acidity/basicity of the amino sugars.

To the best of our knowledge, a systematic survey of simple, partially protected hexopyranosides has not been performed, and quantification of the sugar hydroxy group acidity in partially protected saccharides is still a matter of conjecture.[17]

Determination of the acidic behaviour in the high-alkalinity region, where quick and routine methods such as potentiometry with glass electrodes do not give reliable data, is an independent and rather complex problem. Very weak acids, e.g. alcohols, have often been studied by conductometry[18] or in binary mixtures with subsequent extrapolation.[19]

A highly sensitive comparative method was developed by Hine and Hine.[20] Originally, relative acidities of aliphatic alcohols and polyols were determined spectrophotometrically in isopropyl alcohol as the solvent with *p*-nitrodiphenylamine as the indicator in this "accurate and reliable work".[21] As partially methylated glycopyranosides are also soluble in 2-propanol, this method appeared to be suitable to access the first elucidation of the acidic behaviour of carbohydrate hydroxy groups.

Results and Discussion

As glucose is the most frequent unit in nature, all partially methylated methyl α-D-glucopyranosides **1**–**14** were selected for these studies (Figure 1). Additionally, glucose epimers such as galactose and mannose as well as anomers **15**–**20** were synthesized in order to estimate stereochemical effects (Figure 2).

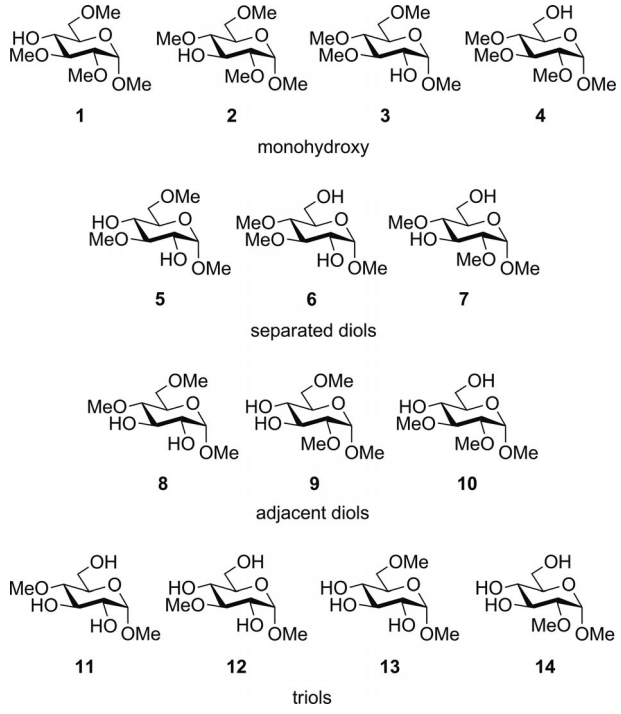


Figure 1. Compounds **1**–**14**.

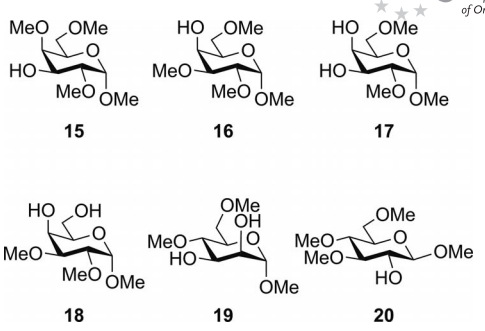
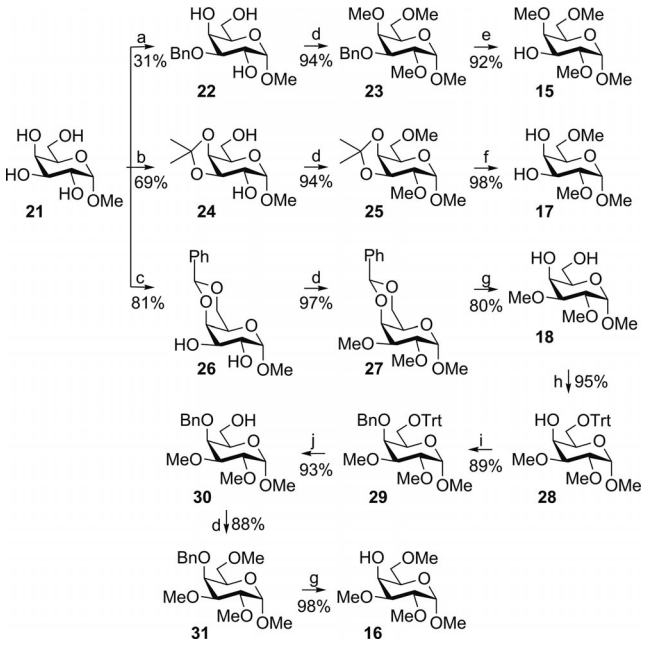


Figure 2. Compounds **15**–**20**.

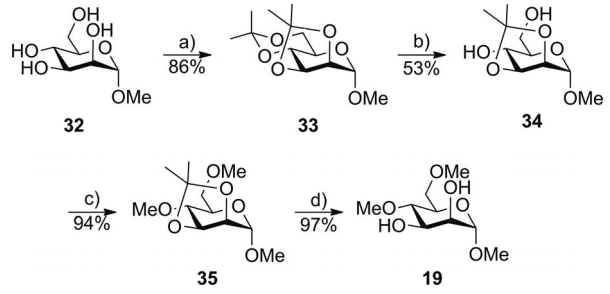
The synthesis of partially methylated methyl α-D-glucopyranosides **1**–**14** has been described previously.[11,12] The preparation of **15**–**20** is shown in Schemes 1, 2 and 3.



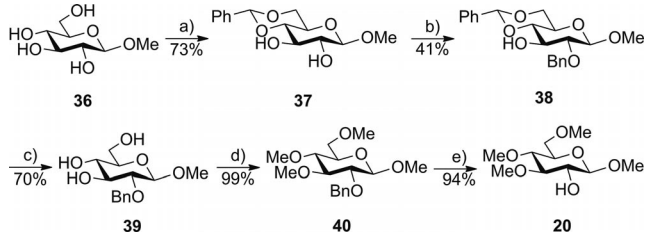
Scheme 1. Synthesis of **15**–**18**: a) Bu_2SnO, toluene, room temp. 17 h; BnBr, 100 °C, 22 h; b) acetone, 2,2′-dimethoxypropane, CSA, room temp., 1.5 h; c) BADMA, CSA, CH_3CN, 80 °C, 20 min; d) 1. NaH (2 equiv. each OH), *N*,*N*-dimethylformamide (DMF), 0–5 °C, 1 h; 2. MeI (2 equiv. each OH), DMF, 0 °C to room temp., 24 h; e) H_2, Pd/C, MeOH, room temp., 72 h; f) 0.2 N HCl, MeOH, 60 °C, 3 h; g) 1 N HCl, H_2O, MeOH, 60 °C, 3 h; h) Trityl chloride, cat. 4-*N*,*N*-dimethylaminopyridine (DMAP), pyridine, 60 °C, 72 h; i) 1. NaH (2 equiv.), DMF, 0–5 °C, 1 h; 2. BnBr (2 equiv.), DMF, 0 °C to room temp., 24 h; j) trifluoroacetic acid (90%), room temp., 5 min.

The 3-OH-free **15** was prepared from **21**, which was benzylated selectively to give **22** by stannylidene activation followed by methylation to **23** and removal of the benzyl group. Derivative **17** was obtained by employing the 3,4-*O*-isopropylidene group as the temporary protecting group. The synthesis of **16** was accomplished in eight steps with **18** as an intermediate (Scheme 1).[11]

Compound **19** was synthesized from the corresponding methyl mannopyranoside **32**, which was converted into the 2,3:4,6-di-*O*-isopropylidene-protected intermediate **33** fol-



Scheme 2. Synthesis of **19**: a) acetone, 2,2′-dimethoxypropane, CSA, 50 °C, 2 h; b) H_2O/AcOH, 4:1, room temp., 7 h; c) 1. NaH (2 equiv. each OH), DMF, 0–5 °C, 1 h; 2. MeI (2 equiv. each OH), DMF, 0 °C to room temp., 24 h; d) 0.2 N HCl, H_2O, MeOH, room temp., 48 h.



Scheme 3. Synthesis of **20**: a) BADMA, CSA, CH_3CN, 80 °C, 20 min; b) BnBr, CH_2Cl_2, 5% NaOH, $Bu_4N^+HSO_4^-$, reflux, 72 h; c) 1 N HCl, H_2O, MeOH, 60 °C, 3 h; d) 1. NaH (2 equiv. each OH), DMF, 0–5 °C, 1 h; 2. MeI (2 equiv. each OH), DMF, 0 °C to room temp., 24 h; e) H_2, Pd/C, MeOH, room temp., 72 h.

lowed by selective removal of the less stable acetal.[27] Treatment of **34** with NaH and MeI in DMF gave **35**, which was deprotected at OH-2 and OH-3 under acidic conditions.

The synthesis of the 3,4,6-tri-*O*-methylated methyl β-D-glucopyranoside **20** (Scheme 3) started from methyl β-D-glucopyranoside (**36**) via intermediates **37** and **38** employing known procedures.[26,28] Furthermore, cleavage of the benzylidene group led to intermediate **39**, which was methylated. Finally, debenzylation of **40** afforded **20** in high yield.

Relative acidities were determined in 2-propanol as the solvent by the indicator method using *p*-nitrodiphenylamine. The equilibrium constant K_e is defined by Equation (1).

$$K_e = [A^-]/[HA][i\text{PrO}^-] \quad (1)$$

K_e was determined by comparing the optical densities of two solutions that contained the same concentration of indicator and base and one of which also contained a certain concentration of the sugar.

Intriguing results for the relative acidities of **1**–**20** (Table 1) were obtained, which elucidate the complex sugar hydroxy group acidic properties. Initially, the results for **1**–**14** will be discussed (Scheme 4).

Table 1. K_e values of **1**–**20** in ascending order.

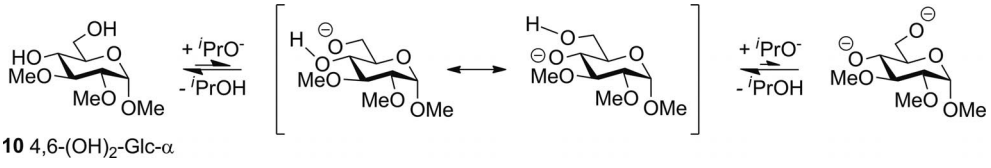
Compound	K_e	Compound	K_e
15 (3-OH-Gal-α)[a]	7.3 ± 0.5	**10** [4,6-$(OH)_2$-Glc-α][b]	100 ± 2
7 [3,6-$(OH)_2$-Gal-α][a]	8.1 ± 0.5	**12** [2,4,6-$(OH)_3$-Glc-α][b]	103 ± 2
1 (4-OH-Glc-α)[a]	8.7 ± 0.8	**17** [3,4-$(OH)_2$-Gal-α][b]	143 ± 4
2 (3-OH-Glc-α)[a]	10.6 ± 0.2	**9** [3,4-$(OH)_2$-Glc-α][b]	150 ± 4
3 (2-OH-Glc-α)[a]	14.2 ± 0.8	**8** [2,3-$(OH)_2$-Glc-α][b]	171 ± 7
4 (6-OH-Glc-α)[a]	16.6 ± 0.6	**11** [2,3,6-$(OH)_3$-Glc-α][b]	171 ± 9
6 [2,6-$(OH)_2$-Glc-α][a]	16.7 ± 0.9	**18** [4,6-$(OH)_2$-Gal-α][b]	207 ± 8
5 [2,4-$(OH)_2$-Glc-α][a]	16.8 ± 0.6	**19** [2,3-$(OH)_2$-Man-α][b]	464 ± 20
20 (2-OH-Gal-β)[a]	17.5 ± 1.3	**14** [3,4,6-$(OH)_3$-Glc-α][c]	507 ± 32
16 (4-OH-Gal-α)[a]	22.7 ± 1.4	**13** [2,3,4-$(OH)_3$-Glc-α][c]	568 ± 27

[a] With separated hydroxy groups. [b] With adjacent hydroxy groups of 1,2- and 1,3-diol types. [c] With adjacent hydroxy groups of 1,2,3- and 1,2,4-triol types.

Small differences in the K_e values of monohydroxy derivatives **1**–**4** were revealed. After deprotonation, the negative charge is located entirely at an oxygen atom that has no stabilizing effect. However, due to different substitution patterns, an acidity order for **1**–**4** was elucidated in which **4** with a primary 6-hydroxy group is the strongest acid due to the more remote position from the electron-withdrawing substituents on the sugar ring. The pK_a of the corresponding 6-amino groups were observed to be more acidic as well.[16] Compounds **1**–**3** are all of the secondary type, which have two β-hydroxy groups and are hence weaker acids. Compound **3** (2-OH) is deprotonated more easily than **2** (3-OH) and **1** (4-OH), most likely due to the proximity to the anomeric centre with more electron-withdrawing capacity. Accordingly, the ascending order of the K_e values for **1**–**4** is: 4-OH < 3-OH < 2-OH < 6-OH.

The order correlates well with Brewster's calculations on the deprotonation enthalpies in α-D-glucopyranose.[15] However, comparing the scale with amino pK_a values (4-NH_2 < 2-NH_2 < 3-NH_2 < 6-NH_2), the 3-positon is suggested to be more acidic than the 2-position. The difference in the K_e value scale is probably caused by hydrogen bonding effects, which are possible in the amino compounds but not in **1**–**4**.[16]

K_e measurements of dihydroxy compounds **5**–**10** revealed two types of acidic behaviour. Compounds, in which hydroxy groups are isolated (**5**–**7**) possess K_e values in the range of monohydroxy compounds.



10 4,6-$(OH)_2$-Glc-α

Scheme 4. Acid–base equilibrium of **10**, which implies intramolecular hydrogen bonding after the first deprotonation.

The lower K_e value of **7** compared to **2**, **4** and **6** shows that the acidity of 3-OH is obviously affected by a free OH-6 and/or vice versa. A corresponding observation was found in the analyses of the pK_a values of diamino sugars.[16]

In contrast, **8**–**10** exhibit significantly increased K_e values. Deprotonation of the diol structures is apparently not the same as for **5**–**7**. An explanation for this phenomenon could be that diol structures are capable of hydrogen bonding. Thus, after the first deprotonation, the negative charge is dispersed and stabilized by mesomeric effects, hence the first proton abstraction is more facile (Scheme 1). Thus, hydrogen bonding in diol structures affects the acidity of the hydroxy groups, and selective deprotonation is excluded.

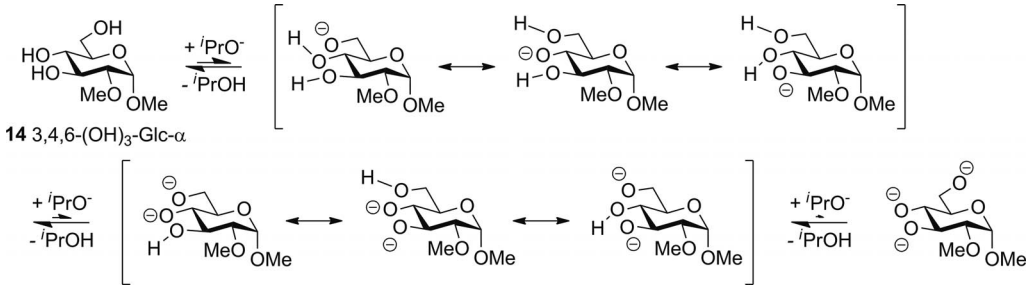
The diol system is more acidic per se concerning monodeprotonation. A second deprotonation is less probable and would lead to a dianionic species, which would result in electronic repulsion and lower solubility.

Furthermore, the K_e values of **8**–**10** show differences between them. Compound **10** is a 1,3-diol, and **8** and **9** exhibit vicinal diol structures with different substitution patterns. In **10**, the efficiency of hydrogen bonding is diminished probably because the distance between 4- and 6-OH is longer than in the 1,2-diol structures. Compound **8** (2,3-diol) shows a higher K_e value than **9** (3,4-diol) because of the proximity to the anomeric centre as already observed in monohydroxy compounds.

A corresponding explanation can be applied to **11**–**14** (Scheme 5). Compounds **11** (2,3,6-triol) and **12** (2,4,6-triol) exhibit K_e values related to **8** (2,3-diol) and **9** (3,4-diol), respectively. Apparently, an additional nonvicinal hydroxy group does not influence the relative acidity constant. In such compounds monodeprotonation of adjacent hydroxy groups occurs predominantly. In contrast, a third adjacent hydroxy group has a noticeable effect on the acid–base equilibrium considering that after first deprotonation the negative charge could be dispersed over three oxygen atoms (Scheme 2).

In general, the more adjacent hydroxy groups a partially methylated derivative has, the larger is its relative acidity in 2-propanol (Figure 3).

In order to detect the influence of stereochemistry on the acidity behaviour, the relative acidity of **15**–**20** were determined. In **20** (2-OH-β) a methyl β-glycopyranoside is present, and **15** (3-OH-Gal) contains an axial OMe at the 4-position. Compounds **16**–**19** exhibit axial hydroxy groups at C-2 and C-4. The obtained K_e values were compared with relative acidities of the corresponding glucose derivatives. It was observed that 2-OH is more acidic if the methyl glucoside has β configuration (cf. **3** and **20**).[13] Furthermore, the axial hydroxy groups in **16** (4-OH-Gal), **18** (4,6-diol-Gal) and especially **19** (2,3-diol-Man) led to an increase in K_e in comparison with the corresponding glucose derivatives **1**, **10** and **8**. Thus, it can be suggested that hydroxy groups are more electron withdrawing when positioned axially at C-2 and C-4 rather than equatorially,[22,23] which is also generally observed in amino sugars.[16] However, by comparison of the 3,4-diols **17** and **9**, there is obviously a deviation from the aforementioned trend, which



Scheme 5. Acid–base equilibrium of **14**, which implies intramolecular hydrogen bonding.

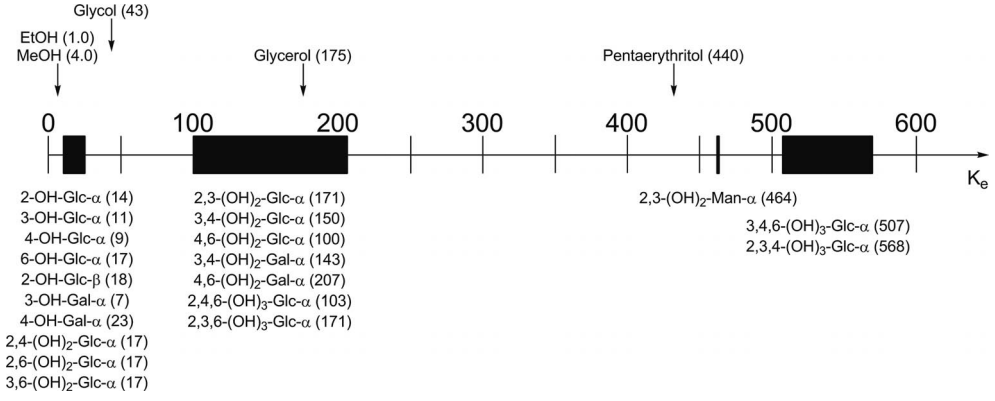


Figure 3. Partially methylated methyl α-D-glycopyranosides, aliphatic alcohols and polyols on a K_e scale. As observed in aliphatic alcohols and polyols, the K_e values of **1**–**20** escalate with the number of adjacent hydroxy groups.

cannot yet be rationalized. Furthermore, an axial methoxy group at C-4 apparently decreases the acidity of OH-3 (cf. **2** and **15**).

It was of particular interest to indicate the pK_a region of partially methylated glycopyranosides. As the K_e and pK_a values of aliphatic alcohols and polyols are known (Table 2), pK_a was plotted against pK_e [log(K_e)] to obtain a linear relationship that allows a qualitative comparison (Figure 4). Thus, the pK_a values of **1**–**20** were calculated from the equation derived from the linear fit. The pK_a values for separated hydroxyl groups in **1**–**7**, **15**, **16** and **20** are 15.0–15.3; for compounds that exhibit adjacent hydroxyl groups of the 1,2- and 1,3-diol type (**8**–**12** and **17**–**18**), the pK_a values are 14.3–14.5; derivatives with three adjacent hydroxy groups (**13**, **14**) and **19**, as an exceptional case, have a pK_a value of around of 14.0.

Table 2. K_e and pK_a values of alcohols, polyols and **1**–**20**.

Compound	K_e	pK_a
Ethanol	1.0[a]	15.9[b]
Methanol	4.0[a]	15.5[b]
1–**7**, **15**, **16**, **20**	7–23	≈ 15.0–15.3
Ethylene glycol	43[a]	14.8[c]
Glycerol	175[a]	14.4[c]
8–**12**, **17**, **18**	100–207	≈ 14.3–14.5
Pentaerythritol	440[a]	14.1[c]
13, **14**, **19**	464–568	≈ 14.0

[a] Ref.[20] [b] Ref.[21] [c] Ref.[24]

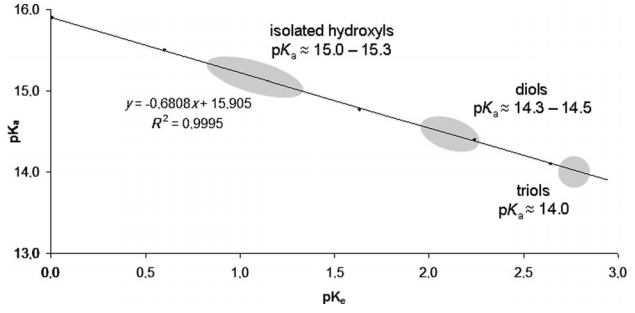


Figure 4. Correlation/linear relationship between the pK_a and pK_e values of aliphatic alcohols and polyols and assignments of the pK_a values of **1**–**20**.

Concerning the relative acidities of separate 2-OH and 3-OH after the first deprotonation of **8** (2,3-diol), the negative charge is located most likely on the 2-position due to the more stable anion. Consequently, the 2-position acts predominantly as a hydrogen-bond acceptor, which should enhance the reactivity at this position. In contrast, hydrogen-bond donation by the 3-position should decrease its reactivity.[3,4] Thus, 2-positions in 2,3-diols and 6-positions in 4,6-diols, respectively, should be more reactive, whereas the reactivity will be similar in 3,4-diols. It can be assumed that deprotonation does not occur completely on addition of excess base in substitution reactions. Therefore, hydrogen bonding will emerge, and the preferred conversion is predicted at O-2 in **8**, **11**, **13** and **19** and at O-6 in **10**, **12**, **14** and **18**. Effectively, this has been observed in the base-promoted glycosylations of partially protected acceptors.[11,12]

Conclusions

The first fundamental acidity studies on partially protected glycopyranosides were performed. Employing a spectrophotometric method, the relative acidities (K_e) for twenty partially methylated glycopyranosides were determined, and a first estimation of the pK_a values performed. It was proven that the more adjacent hydroxy groups a sugar displays, the more acidic is the corresponding hydroxy system. Diol and triol structures show extended hydrogen bonding. The results for partially methylated glucopyranose epimers and anomers revealed the influence of the stereochemistry on the relative acidity.

Experimental Section

Chemicals and Solvents: The synthesis of **1**–**14** was described previously.[11,12] Intermediates **22**,[25] **26**,[26] **33**,[27] **34**,[27] **37**[26] and **38**[28] were prepared as described. The remaining intermediates and target compounds **15**–**20** were prepared according to the general procedures previously described[12] except for **17**, **19** and **24**, the preparation of which is described below. NMR spectra for **15**–**20** and **24**, **25**, **27**–**31**, **35**, **39** and **40** are given in the Supporting Information. 4-Nitrodiphenylamine (≥ 99%) and 2-propanol (≥ 99.5%, absolute, over molecular sieve) were of commercial origin. Sodium isopropanolate was prepared freshly before the measurements by the addition of sodium (approx. 100 mg) to 2-propanol (50 mL).

Determination of K_e in 2-Propanol: The K_e values of **1**–**20** were determined according to the procedure published by Hine and Hine.[20] This method is based on the comparison of the optical densities of two solutions that contain identical concentrations of indicator and base and one of which also contains a certain concentration of the partially protected glycopyranoside. The blind experiment (without the sugar) was performed as follows: 2-propanol (1 mL) and indicator solution (1 mL) were combined in a flask. After stirring, sodium isopropanolate solution (1 mL) was added, the mixture stirred again and 1 mL of the mixture was transferred into a spectrophotometer cell. Between addition of the base and determination of optical density, exactly 60 seconds passed. An analogous procedure was performed for the experiment that contained the sugar: Specified amounts of **1**–**20** were dissolved in 2-propanol (1 mL). Subsequently, indicator solution (1 mL) was added, the solution was stirred and base solution (1 mL) was added. The optical density was measured after stirring and transfer of the solution to a spectrophotometric cell. The optical density readings were mainly in the range of 0.3–0.6 at 500 nm. Additions of corresponding solutions were performed with the same pipette. The final solutions were about 10^{-4} M of indicator and 0.003–0.05 M of the sugar, depending upon acidity. The basicity of the *i*PrONa/*i*PrOH solution was adapted to obtain an optical density of approximately 0.6 for the blind experiment. K_e was calculated with the following equations:[20]

$$\left[i\mathrm{Pr}\,\mathrm{O}^-\right]_{init} = \frac{OD_{init} - \varepsilon_{HIn}\cdot\left[HIn\right]}{K_1\left(\left[HIn\right]\cdot\varepsilon_{In^-} - OD_{init}\right)}$$

$$\left[i\mathrm{Pr}\,\mathrm{O}^-\right]_{final} = \frac{OD_{final} - \varepsilon_{HIn}\cdot\left[HIn\right]}{K_1\left(\left[HIn\right]\cdot\varepsilon_{In^-} - OD_{final}\right)}$$

$$K_e = \frac{\left[i\mathrm{Pr}\,\mathrm{O}^-\right]_{init} - \left[i\mathrm{Pr}\,\mathrm{O}^-\right]_{final}}{\left(\left[HA\right] - \left[i\mathrm{Pr}\,\mathrm{O}^-\right]_{init} + \left[i\mathrm{Pr}\,\mathrm{O}^-\right]_{final}\right)\cdot\left[i\mathrm{Pr}\,\mathrm{O}^-\right]_{final}}$$

All parameters to calculate K_e are summarized in the Supporting Information.

For each investigated compound, six to eight K_e values were measured at different concentrations. The accuracy was quantified by standard deviation and is in all cases below 10%. Detailed experimental results for **1**–**20** are given in the Supporting Information.

Methyl 2,4,6-Tri-*O*-methyl-α-D-galactopyranoside (15): Cleavage of the benzyl group was performed according to ref.[12] Compound **23** (1.51 g, 4.63 mmol), Pd(10%)/C (100 mg), MeOH (50 mL); yield 92% (1.00 g, 4.25 mmol), colourless solid, R_f = 0.20 [ethyl acetate (EA)], m.p. 69 °C, $[\alpha]_D^{25}$ = +131.0 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.93 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.00–3.94 (m, 1 H, 3-H), 3.92 (ddd, $^3J_{4,5}$ = 0.9, $^3J_{5,6a}$ = 6.3, $^3J_{5,6b}$ = 6.3 Hz, 1 H, 5-H), 3.62 (dd, $^3J_{3,4}$ = 3.6, $^3J_{4,5}$ = 0.9 Hz, 1 H, 4-H), 3.58–3.53 (m, 2 H, 6-H) 3.51 (dd, $^3J_{1,2}$ = 3.5, $^3J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 2.39–2.31 (s, 1 H, O*H*-3), 3.59, 3.50, 3.43, 3.41 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 97.2 (C-1), 79.0 (C-4), 78.9 (C-2), 71.3 (C-6), 70.2 (C-3), 68.9 (C-5), 61.7, 59.2, 58.2, 55.4 (O*C*H_3) ppm. HRMS (ESI): calcd. for $C_{10}H_{20}O_6$ [M + Na]$^+$ 259.1152; found 259.1152.

Methyl 2,3,6-Tri-*O*-methyl-α-D-galactopyranoside (16): Cleavage of the benzyl group was performed according to ref.[12] Compound **31** (2.11 g, 6.46 mmol), Pd(10%)/C (77 mg), MeOH (50 mL); yield 98% (1.49 g, 6.31 mmol), colourless syrup, R_f = 0.19 (EA), $[\alpha]_D^{25}$ = +154.5 (c = 0.2, H_2O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.91 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.12 (dd, $^2J_{3,4}$ = 3.3, $^3J_{4,5}$ = 1.3 Hz, 1 H, 4-H), 3.90–3.85 (m, 1 H, 5-H), 3.69–3.65 (m, 2 H, 6-H), 3.60 (dd, $^3J_{1,2}$ = 3.5, $^3J_{2,3}$ = 9.8 Hz, 1 H, 2-H), 3.56–3.51 (m, 1 H, 3-H), 3.51, 3.50, 3.44, 3.43 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 97.9 (C-1), 79.2 (C-3), 77.3 (C-2), 72.3 (C-6), 68.2 (C-5), 67.1 (C-4), 59.4, 59.0, 57.7, 55.3 (O*C*H_3) ppm. HRMS (ESI): calcd. for $C_{10}H_{20}O_6$ [M + Na]$^+$ 259.1152; found 259.1154.

Methyl 2,6-Di-*O*-methyl-α-D-galactopyranoside (17): Compound **25** (1.64 g, 6.25 mmol) was dissolved in MeOH (50 mL), 0.2 N HCl (1 mL) was added, and the mixture was heated to reflux for 3 h, neutralized with saturated $NaHCO_3$ solution and concentrated under reduced pressure. The product was purified by flash column chromatography (gradient petroleum ether/EA); yield 98% (1.37 g, 6.16 mmol), colourless syrup, R_f = 0.17 (EA), $[\alpha]_D^{25}$ = +150.8 (c = 0.64, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.96 (d, $^3J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 4.08–4.04 (m, 1 H, 4-H), 3.94–3.89 (m, 1 H, 3-H), 3.89–3.86 (m, 1 H, 5-H), 3.70–3.67 (m, 2 H, 6-H), 3.56 (dd, $^3J_{1,2}$ = 3.4, $^3J_{2,3}$ = 9.7 Hz, 1 H, 2-H), 3.49, 3.43, 3.42 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 97.3 (C-1), 78.3 (C-2), 72.8 (C-6), 70.1 (C-4), 69.4 (C-3), 68.2 (C-5), 59.5, 58.2, 55.4 (O*C*H_3) ppm. HRMS (ESI): calcd. for $C_9H_{18}O_6$ [M + Na]$^+$ 245.0996; found 245.0994.

Methyl 2,3-Di-*O*-methyl-α-D-galactopyranoside (18): Cleavage of the benzylidene group was performed according to ref.[12] Compound **27** (4.00 g, 12.9 mmol), MeOH (80 mL), H_2O (8 mL), 1 N HCl (1 mL); yield 80% (2.28 g, 10.3 mmol), colourless syrup, R_f = 0.10 (EA), $[\alpha]_D^{25}$ = +145.5 (c = 0.2, $CHCl_3$) {ref.[29] $[\alpha]_D^{25}$ = +167 ($CHCl_3$)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.92 (d, $^3J_{1,2}$ = 3.3 Hz, 1 H, 1-H), 4.17–4.15 (m, 1 H, 4-H), 3.96 (dd, $^3J_{5,6a}$ = 5.6, $^2J_{6a,6b}$ = 11.4 Hz, 1 H, 6a-H), 3.84 (dd, $^3J_{5,6b}$ = 4.3, $^2J_{6a,6b}$ = 11.4 Hz, 1 H, 6b-H), 3.81–3.76 (m, 1 H, 5-H), 3.59 (dd, $^3J_{1,2}$ = 3.3, $^3J_{2,3}$ = 9.6 Hz, 1 H, 2-H), 3.54 (dd, $^3J_{2,3}$ = 9.6, $^3J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.51, 3.50, 3.43 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 97.8 (C-1), 79.0 (C-3), 77.3 (C-2), 69.0 (C-5), 67.9 (C-4), 63.0 (C-6), 58.9, 57.8, 55.3 (O*C*H_3) ppm. HRMS (ESI): calcd. for $C_9H_{18}O_6$ [M + Na]$^+$ 245.0996; found 245.0995.

Methyl 4,6-Di-*O*-methyl-α-D-mannopyranoside (19): Compound **35** (1.94 g, 7.40 mmol) was dissolved in MeOH (30 mL), 0.2 N HCl (1 mL) was added, and the mixture was stirred at room temperature for 48 h, neutralized with saturated $NaHCO_3$ solution and concentrated under reduced pressure. The product was purified by flash column chromatography (gradient petroleum ether/EA); yield 97% (1.59 g, 7.15 mmol), colourless syrup, R_f = 0.12 (EA); $[\alpha]_D^{25}$ = +84.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.72 (d, $^3J_{1,2}$ = 1.4 Hz, 1 H, 1-H), 3.93–3.88 (m, 1 H, 2-H), 3.88–3.81 (m, 1 H, 3-H), 3.67–3.57 (m, 2 H, 6-H), 3.60–3.56 (m, 1 H, 5-H), 3.44 (dd, $^3J_{3,4}$ = 9.3, $^3J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.55, 3.43, 3.37 (s, 3 H, OCH_3), 2.75–2.70 (m, 2 H, O*H*-2, O*H*-3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 100.7 (C-1), 77.4 (C-4), 71.7 (C-3), 71.4 (C-6), 71.0 (C-2), 70.4 (C-5), 60.6, 59.2, 55.0 (O*C*H_3) ppm. HRMS (ESI): calcd. for $C_9H_{18}O_6$ [M + Na]$^+$ 245.0996; found 245.1001. HRMS (FAB): calcd. for $C_9H_{18}O_6$ [M + H]$^+$ 223.1176; found 223.1182.

Methyl 3,4,6-Tri-*O*-methyl-β-D-glucopyranoside (20): Cleavage of the benzyl group was performed according to ref.[12] Compound **40** (877 mg, 2.69 mmol), Pd(10%)/C (107 mg), MeOH (50 mL); yield 94% (598 mg, 2.53 mmol), colourless solid, R_f = 0.29 (EA), m.p. 50–51 °C (ref.[30] m.p. 51–52 °C), $[\alpha]_D^{25}$ = –19.5 (c = 0.2, $CHCl_3$) {ref. 30 $[\alpha]_D^{25}$ = –20 ($CHCl_3$)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.14 (d, $^3J_{1,2}$ = 7.8 Hz, 1 H, 1-H), 3.66 (dd, $^3J_{5,6a}$ = 2.0, $^2J_{6a,6b}$ = 10.5 Hz, 1 H, 6a-H), 3.58 (dd, $^3J_{5,6b}$ = 4.4, $^2J_{6a,6b}$ = 10.5 Hz, 1 H, 6b-H), 3.42–3.36 (m, 1 H, 2-H), 3.36–3.30 (m, 1 H, 5-H), 3.25–3.16 (m, 2 H, 4-H, 3-H) 3.66, 3.54, 3.54, 3.41 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 103.6 (C-1), 86.0 (C-3), 79.4 (C-4), 75.0 (C-5), 74.0 (C-2), 71.2 (C-6), 60.7, 60.3, 59.3, 57.1 (O*C*H_3) ppm. HRMS (ESI): calcd. for $C_{10}H_{20}O_6$ [M + Na]$^+$ 259.1152; found 259.1155.

Methyl 3,4-*O*-Isopropylidene-α-D-galactopyranoside (24): Compound **21** (3.05 g, 15.7 mmol) was suspended in dry acetone (80 mL), 2,2′-dimethoxypropane (4.0 mL, 39 mmol) and CSA (0.2 g, 0.8 mmol) were added. After 1.5 h the mixture was neutralized with NEt_3 and concentrated. The product was purified by flash column chromatography (gradient petroleum ether/EA); yield 69% (2.52 g, 10.8 mmol), colourless solid, R_f = 0.24 (EA), m.p. 105 °C (ref.[31] m.p. 97–98 °C), $[\alpha]_D^{25}$ = +132.4 (c = 0.5, $CHCl_3$) {ref.[31] $[\alpha]_D^{25}$ = +135 (c = 1.61, $CHCl_3$)}. ^{1}H NMR (400 MHz, MeOD): δ = 4.64 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.24 (dd, $^3J_{3,4}$ = 5.5, $^3J_{4,5}$ = 2.5 Hz, 1 H, 4-H), 4.12 (dd, $^3J_{2,3}$ = 7.7, $^3J_{3,4}$ = 5.5 Hz, 1 H; 3-H), 4.03–3.98 (m, 1 H, 5-H), 3.76–3.73 (m, 2 H, 6-H), 3.62 (dd, 1 H, 2-H), 3.41 (s, 3 H, OCH_3), 1.46, 1.32 (s, 3 H, CH_3) ppm. ^{13}C NMR (101 MHz, MeOD): δ = 110.4 [$(CH_3)_2C$OO], 101.2 (C-1), 77.9 (C-3), 74.9 (C-4), 71.6 (C-2), 69.7 (C-5), 62.7 (C-6), 55.9 (O*C*H_3), 28.5, 26.5 (*C*H_3) ppm.

Methyl 3,4-*O*-Isopropylidene-2,6-di-*O*-methyl-α-D-galactopyranoside (25): Methylation of the hydroxy groups was performed according to ref.[12] Compound **24** (1.56 g, 6.66 mmol), NaH (640 mg,

16.0 mmol), MeI (1.6 mL, 25.7 mmol), absolute DMF (50 mL); yield 94% (1.64 g, 6.25 mmol), colourless syrup, R_f = 0.27 (petroleum ether/EA, 1:1), $[\alpha]_D^{25}$ = +157.8 (c = 0.5, $CHCl_3$) {ref.[32] $[\alpha]_D^{25}$ = +142 (c = 1.7, $CHCl_3$)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.84 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.24 (dd, $^3J_{2,3}$ = 7.8 Hz, $^3J_{3,4}$ = 5.5 Hz, 1 H, 3-H), 4.14 (dd, $^3J_{3,4}$ = 5.5 Hz, $^3J_{4,5}$ = 2.6 Hz, 1 H, 4-H), 4.13–4.08 (m, 1 H, 5-H), 3.67–3.63 (m, 2 H, 6-H), 3.51, 3.42, 3.41 (s, 3 H, OCH_3) 3.34 (dd, $^3J_{1,2}$ = 3.5 Hz, $^3J_{2,3}$ = 7.8 Hz, 1 H, 2-H), 1.52, 1.32 (s, 3 H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 109.2 [$(CH_3)_2C$OO], 97.7 (C-1), 79.3 (C-2), 75.9 (C-3), 73.8 (C-4), 72.1 (C-6), 66.4 (C-5), 59.3, 58.7, 55.5 (OCH$_3$), 28.3, 26.3 (CH$_3$) ppm.

Methyl 4,6-*O*-Benzylidene-2,3-di-*O*-methyl-α-D-galactopyranoside (27): Methylation of the hydroxy groups was performed according to ref.[12] Compound **26** (4.00 g, 14.2 mmol), NaH (2.56 g, 64.0 mmol), MeI (4.0 mL, 64 mmol), absolute DMF (60 mL); yield 97% (4.28 g, 13.8 mmol), colourless solid, R_f = 0.42 (EA), m.p. 114–115 °C (ref.[29] m.p. 123–124 °C), $[\alpha]_D^{25}$ = +162.3 (c = 0.21, $CHCl_3$) {ref.[29] $[\alpha]_D^{25}$ = +170 ($CHCl_3$)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.51 (m, 2 H, H$_{arom.}$), 7.40–7.31 (m, 3 H, H$_{arom.}$), 5.56 (s, 1 H, PhCHOO), 5.01 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.38–4.34 (m, 1 H, 4-H), 4.28 (dd, $^3J_{5,6a}$ = 1.2, $^2J_{6a,6b}$ = 12.6 Hz, 1 H, 6a-H), 4.09 (dd, $^3J_{5,6b}$ = 1.3, $^2J_{6a,6b}$ = 12.6 Hz, 1 H, 6b-H), 3.81 (dd, $^3J_{1,2}$ = 3.5, $^3J_{2,3}$ = 10.1 Hz, 1 H, 2-H), 3.70 (dd, $^3J_{2,3}$ = 10.1, $^3J_{3,4}$ = 3.5 Hz, 1 H, 3-H), 3.67–3.64 (m, 1 H, 5-H), 3.54, 3.53, 3.46 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.6 (C$_{arom.}$), 128.9, 128.1, 126.4 (CH$_{arom}$), 101.3 (PhCHOO), 98.6 (C-1), 77.5 (C-3), 77.3 (C-2), 73.8 (C-4), 69.4 (C-6), 62.6 (C-5), 59.1, 57.8, 55.5 (OCH$_3$) ppm.

Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (28): Tritylation of OH-6 was performed according to ref.[12] Compound **18** (2.2 g, 10 mmol), chlorotriphenylmethane (3.1 g, 11 mmol), catalytic amount of DMAP (approx. 20 mg), pyridine (30 mL); yield 95% (4.5 g, 9.6 mmol), colourless solid, R_f = 0.53 (EA), m.p. 70–71 °C (ref.[33] m.p. 77–80 °C), $[\alpha]_D^{25}$ = +70.5 (c = 0.2 in $CHCl_3$) {ref.[33] $[\alpha]_D^{25}$ = +68.0 ($CHCl_3$)}. ^{1}H NMR (400 MHz, MeOD): δ = 7.50–7.42 (m, 6 H, H$_{arom.}$), 7.33–7.19 (m, 9 H, H$_{arom.}$), 4.91 (d, $^3J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.02–3.98 (m, 1 H, 4-H), 3.82–3.76 (m, 1 H, 5-H), 3.54 (dd, $^3J_{1,2}$ = 3.8 Hz, $^3J_{2,3}$ = 10.1 Hz, 1 H, 2-H), 3.44–3.38 (m, 2 H, 3-H, 6a-H), 3.23 (dd, $^3J_{5,6b}$ = 4.6 Hz, $^2J_{6a,6b}$ = 10.0 Hz, 1 H, 6b-H), 3.46, 3.45, 3.40 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, MeOD): δ = 145.7 (C$_{arom.}$), 130.0, 128.9, 128.3 (CH$_{arom.}$), 99.0 (C-1), 88.2 (Ph$_3C$O), 80.8 (C-3), 78.9 (C-2), 71.1 (C-5), 67.7 (C-4), 65.2 (C-6), 59.0, 57.4, 55.5 (OCH$_3$) ppm. MS (MALDI-TOF): m/z = 488.3 [M + Na]$^+$.

Methyl 4-*O*-Benzyl-2,3-di-*O*-methyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (29): Benzylation of the hydroxy group was performed according to ref.[12] Compound **28** (4.4 g, 9.4 mmol), NaH (940 mg, 23.6 mmol), BnBr (2.80 mL, 23.6 mmol), absolute DMF (45 mL); yield 89% (4.7 g, 8.4 mmol), colourless solid, R_f = 0.14 (petroleum ether/EA, 3:1), m.p. 51–52 °C, $[\alpha]_D^{25}$ = +0.59 (c = 0.21, MeOH). ^{1}H NMR (400 MHz, MeOD): δ = 7.43–7.37 (m, 6 H, H$_{arom.}$), 7.32–7.18 (m, 12 H, H$_{arom.}$), 7.13–7.08 (m, 2 H, H$_{arom.}$), 4.85 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.72 (d, $^2J_{A,A'}$ = 11.1 Hz, 1 H, OCH_2Ph-A), 4.41 (d, $^2J_{A,A'}$ = 11.1 Hz, 1 H, OCH_2Ph-A′), 3.95 (dd, $^3J_{3,4}$ = 3.0, $^3J_{4,5}$ = 0.8 Hz, 1 H, 4-H), 3.78–3.72 (m, 1 H, 5-H), 3.59 (dd, $^3J_{1,2}$ = 3.5, $^3J_{2,3}$ = 10.4 Hz, 1 H, 2-H), 3.50 (dd, $^3J_{2,3}$ = 10.4, $^3J_{3,4}$ = 3.0 Hz, 1 H, 3-H), 3.43–3.36 (m, 1 H, 6a-H), 3.13 (dd, $^3J_{5,6b}$ = 5.8, $^2J_{6a,6b}$ = 9.9 Hz, 1 H, 6b-H), 3.46, 3.45, 3.41 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, MeOD): δ = 145.5, 139.9 (C$_{arom.}$), 130.0, 129.4, 129.3, 129.0, 128.8, 128.3 (CH$_{arom.}$), 99.1 (C-1), 88.4 (Ph$_3C$O), 81.9 (C-3), 79.5 (C-2), 75.9 (OCH$_2$Ph-A), 75.8 (C-4), 71.1 (C-5), 64.9 (C-6), 59.1, 58.6, 55.5 (OCH$_3$) ppm. HRMS (ESI): calcd. for $C_{35}H_{38}O_6$ [M + Na]$^+$ 577.2561; found 577.2562.

Methyl 4-*O*-Benzyl-2,3-di-*O*-methyl-α-D-galactopyranoside (30): Cleavage of the triphenylmethyl group was performed according to ref.[12] Compound **29** (4.6 g, 8.3 mmol), trifluoroacetic acid (90%, 17 mL); yield 93% (2.4 g, 7.7 mmol), yellow syrup, R_f = 0.31 (EA), $[\alpha]_D^{25}$ = +0.81 (c = 0.29, H_2O). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.30 (m, 5 H, H$_{arom.}$), 4.96 (d, $^2J_{A,A'}$ = 11.8 Hz, 1 H, OCH_2Ph-A), 4.93 (d, $^3J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.63 (d, $^2J_{A,A'}$ = 11.8 Hz, 1 H, OCH_2Ph-A′), 3.95–3.91 (m, 1 H, 4-H), 3.81–3.71 (m, 3 H, 2-H, 5-H, 6a-H), 3.60 (dd, $^3J_{2,3}$ = 10.0, $^3J_{3,4}$ = 2.8 Hz, 1 H, 3-H), 3.57–3.52 (m, 1 H, 6b-H), 3.55, 3.54, 3.42 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.2 (C$_{arom.}$), 128.5, 127.9 (CH$_{arom.}$), 98.0 (C-1), 80.9 (C-3), 78.1 (C-2), 74.5 (OCH$_2$Ph-A), 73.8 (C-4), 70.3 (C-5), 62.5 (C-6), 58.9, 58.6, 55.3 (OCH$_3$) ppm. HRMS (ESI): calcd. for $C_{16}H_{24}O_6$ [M + Na]$^+$ 335.1465; found 335.1470.

Methyl 4-*O*-Benzyl-2,3,6-tri-*O*-methyl-α-D-galactopyranoside (31): Methylation of the hydroxy group was performed according to ref.[12] Compound **30** (2.3 g, 7.4 mmol), NaH (750 mg, 18.8 mmol), MeI (1.2 mL, 19 mmol), absolute DMF (40 mL); yield 88% (2.2 g, 6.6 mmol), colourless syrup, R_f = 0.36 (PE/EA, 1:1), $[\alpha]_D^{25}$ = +110.5 (c = 0.32, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.25 (m, 5 H, H$_{arom.}$), 4.93 (d, $^2J_{A,A'}$ = 11.6 Hz, 1 H, OCH_2Ph-A), 4.91 (d, $^3J_{1,2}$ = 3.8 Hz, 1 H, 1-H), 4.61 (d, $^2J_{A,A'}$ = 11.6 Hz, 1 H, OCH_2Ph-A′), 3.94 (dd, $^3J_{3,4}$ = 2.3, $^3J_{4,5}$ = 1.0 Hz, 1 H, 4-H), 3.88–3.82 (m, 1 H, 5-H), 3.76 (dd, $^3J_{1,2}$ = 3.8, $^3J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 3.58 (dd, $^3J_{2,3}$ = 10.0, $^3J_{3,4}$ = 2.3 Hz, 1 H, 3-H), 3.49–3.41 (m, 2 H, 6-H), 3.53, 3.51, 3.42, 3.31 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.6 (C$_{arom.}$), 128.2, 127.6 (CH$_{arom.}$), 97.8 (C-1), 80.7 (C-3), 77.9 (C-2), 74.7 (OCH$_2$Ph-A), 73.8 (C-4), 71.5 (C-6), 69.1 (C-5), 59.1, 58.8, 58.3, 55.3 (OCH$_3$) ppm. HRMS (ESI): calcd. for $C_{17}H_{26}O_6$ [M + Na]$^+$ 349.1622; found 349.1623.

Methyl 2,3-*O*-Isopropylidene-4,6-di-*O*-methyl-α-D-mannopyranoside (35): Methylation of the hydroxy groups was performed according to ref.[12] Compound **34** (1.88 g, 8.04 mmol), NaH (1.30 g, 32.1 mmol), MeI (2.0 mL, 32 mmol), absolute DMF (40 mL); yield 94% (1.98 g, 7.54 mmol), colourless syrup, R_f = 0.50 (petroleum ether/EA, 1:1), $[\alpha]_D^{25}$ = +42.7 (c = 0.21, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.91 (s, 1 H, 1-H), 4.17 (dd, $^3J_{2,3}$ = 5.8, $^3J_{3,4}$ = 6.8 Hz, 1 H, 3-H), 4.09 (d, $^3J_{2,3}$ = 5.8 Hz, 1 H, 2-H), 3.66–3.56 (m, 3 H, 6-H, 5-H), 3.50, 3.41, 3.38 (s, 3 H, OCH_3), 3.32–3.25 (m, 1 H, 4-H), 1.53, 1.34 (s, 3 H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 109.2 [$(CH_3)_2C$OO], 98.4 (C-1), 78.5 (C-3), 77.8 (C-4), 75.8 (C-2), 71.6 (C-6), 68.1 (C-5), 59.3, 59.2, 54.9 (OCH$_3$), 28.0, 26.2 (CH$_3$) ppm. HRMS (ESI): calcd. for $C_{12}H_{22}O_6$ [M + Na]$^+$ 285.1309; found 285.1313.

Methyl 2-*O*-Benzyl-β-D-glucopyranoside (39): Cleavage of the benzylidene group was performed according to ref.[12] Compound **38** (1.63 g, 4.38 mmol), MeOH (40 mL), H_2O (3 mL), 1 N HCl (1 mL); yield 70% (870 mg, 3.06 mmol), colourless solid, R_f = 0.11 (EA); m.p. 130 °C, $[\alpha]_D^{25}$ = +20.5 (c = 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.29 (m, 5 H, H$_{arom.}$), 4.95 (d, $^2J_{A,A'}$ = 11.4 Hz, 1 H, OCH_2Ph-A), 4.64 (d, $^2J_{A,A'}$ = 11.4 Hz, 1 H, OCH_2Ph-A′), 4.37 (d, $^3J_{1,2}$ = 7.8 Hz, 1 H, 1-H), 3.93 (dd, $^3J_{5,6a}$ = 3.5, $^2J_{6a,6b}$ = 11.8 Hz, 1 H, 6a-H), 3.82 (dd, $^3J_{5,6b}$ = 4.8, $^2J_{6a,6b}$ = 11.8 Hz, 1 H, 6b-H), 3.61–3.53 (m, 2 H, 3-H, 4-H), 3.42–3.35 (m, 1 H, 5-H), 3.23–3.17 (m, 1 H, 2-H), 3.35 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.3 (C$_{arom.}$), 128.6, 128.1, 128.0 (CH$_{arom.}$), 104.6 (C-1), 80.9 (C-2), 76.0 (C-3), 75.0 (C-5), 74.4 (OCH$_2$Ph), 70.5 (C-4), 62.6 (C-6), 57.2 (OCH$_3$) ppm. HRMS (ESI): calcd. for $C_{14}H_{20}O_6$ [M + Na]$^+$ 307.1152; found 307.1158.

Methyl 2-*O*-Benzyl-3,4,6-tri-*O*-methyl-β-D-glucopyranoside (40): Methylation of the hydroxy groups was performed according to

ref.[12] Compound **39** (807 mg, 2.84 mmol), NaH (720 mg, 18.0 mmol), MeI (8.5 mL, 17 mmol, 2 M solution in methyl tertiary butyl ether), absolute DMF (40 mL); yield 99% (924 mg, 2.83 mmol), colourless syrup, R_f = 0.68 (EA), $[\alpha]_D^{25}$ = +13.0 (*c* = 0.27, $CHCl_3$) {ref.[30] $[\alpha]_D^{25}$ = +9.9 ($CHCl_3$)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.24 (m, 5 H, $H_{arom.}$), 4.88 (d, $^2J_{A,A'}$ = 11.1 Hz, 1 H; OCH_2Ph-A), 4.69 (d, $^2J_{A,A'}$ = 11.1 Hz, 1 H, OCH_2Ph-A′), 4.25 (d, $^3J_{1,2}$ = 7.3 Hz, 1 H, 1-H), 3.69–3.63 (m, 1 H, 6a-H), 3.61–3.54 (m, 1 H, 6b-H), 3.33–3.22 (m, 3 H, 5-H, 3-H, 2-H), 3.21–3.14 (m, 1 H, 4-H) 3.63, 3.55, 3.54, 3.42 (s, 3 H, OCH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.7 ($C_{arom.}$), 128.3, 128.0, 127.6 ($CH_{arom.}$), 104.6 (C-1), 86.4 (C-2), 82.0 (C-3), 79.6 (C-4), 74.7 (C-5), 74.6 (OCH_2Ph), 71.4 (C-6), 61.0, 60.4, 59.4, 57.0 (OCH_3) ppm. HRMS (ESI): calcd. for $C_{17}H_{26}O_6$ [M + Na]$^+$ 349.1622; found 349.1625.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all new compounds. K_e values for **1**–**20**.

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Received: November 28, 2011
Published Online: February 27, 2012

