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Note

Allyl deprotection of galacturonic acid derivatives: mechanistic aspects of mercuric-catalyzed prop-1-enyl acetal cleavage

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Abstract—Different deallylation methods were assayed for selective deprotection of allyl galactopyranosiduronic acid derivatives. A two-step procedure using DABCO and $(Ph_3P)_3RhCl$ followed by mercuric-assisted cleavage gave quantitative yields. Reaction in the presence of [^{18}O]water allowed us to obtain evidence about the mechanism of prop-1-enyl cleavage.
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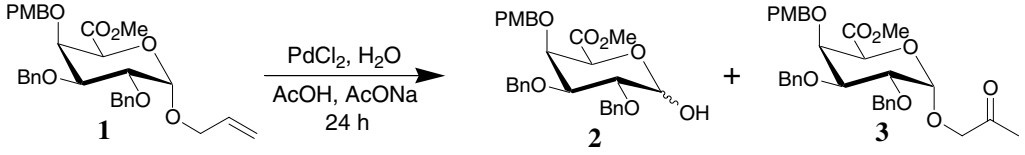
Several methods for deprotection of allyl glycosides are described[1,2] that tolerate a diversity of functional groups. Nonetheless, cleavage of allyl protection of polyfunctional allyl protected carbohydrate acetals is still problematic. Selective cleavage[3] using Pd^{II} has been previously used on oligosaccharides bearing different protecting groups such as esters, acids, amines, amides, phosphates and aromatic substituents.[4–6] Compound **1** was reacted in the conditions previously described[4] ($PdCl_2$/AcOH/AcONa/H_2O). After 24 h, mass spectrometry analysis (ESI+) showed the presence of starting material **1** at $[M+Na]^+ = 571$, and the desired product **2** at $[M+Na]^+ = 531$. A third unexpected compound was detected at $[M+Na]^+ = 587$. The difference of +16 mass units compared to the starting compound **1** suggested the presence of oxidation product **3** (Scheme 1).

All attempts to achieve chromatographic separation of compounds **2** and **3** were unsuccessful, and the mixture was analyzed by NMR. The typical allyl resonances, a dddd for H2′ at $\delta = 5.9$ ppm, and two ddt for H3′ at $\delta = 5.3$ ppm in the ^{1}H NMR spectrum, and at $\delta = 133.5$ ppm (C2′) and $\delta = 118.1$ ppm (C3′) in the ^{13}C NMR spectrum, were completely absent. Instead, new resonances were observed at 2.12 ppm and 205.6 ppm, respectively, confirming the formation of ketone **3**. From the NMR spectra of the mixture, **2**/**3** ratio was estimated as 60/40. As by-product **3** arises from a Wacker-type oxidation of the double bond, the presence of an oxidant in the reaction mixture was suspected. The reaction was repeated using degassed water (by bubbling He), but the same result was obtained.

As the problem could be related to the substrate structure, and compound **1** required multistep synthesis,



Scheme 1.

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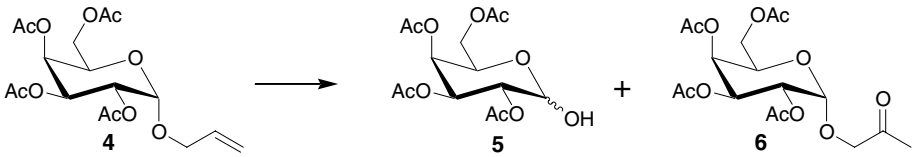


Scheme 2.

different conditions were tested on a simpler starting material, allyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside[7] (**4**). Firstly, the Pd(II) reaction was performed on **4** in the same conditions. Again, the expected product **5** was obtained, together with the oxidized compound **6** (Scheme 2), which was the major product as estimated from NMR spectra of the **5/6** mixture.

Different modifications of the reaction were assayed. The results are summarized in Table 1. Changing the ligands of the Pd(II), by replacing $PdCl_2$ by $Pd(OAc)_2$ (entry 2), did not make any difference. In some examples[5c] the reaction was performed in methanol, in our hands the **5/6** ratio was not improved, either using $Pd(OAc)_2$ or $PdCl_2$ (entries 3 and 4). When a non-protic solvent such as dichloromethane was used (entry 5), no reaction occurred. A bulky alcohol (entry 6) or an amine (entry 7) did not work. A method using a catalytic amount of $PdCl_2$, which is regenerated by CuI, which in turn is obtained by bubbling oxygen into the solution,[8] was assayed (entry 8) with similar results.

Alternative methods have been reported. Pd/C seemed to be only effective on *O*-allyl phenols.[9] Reactions using DDQ[10] or NBS[11] are not applicable to our original substrate **1** bearing *p*-methoxybenzyl groups.

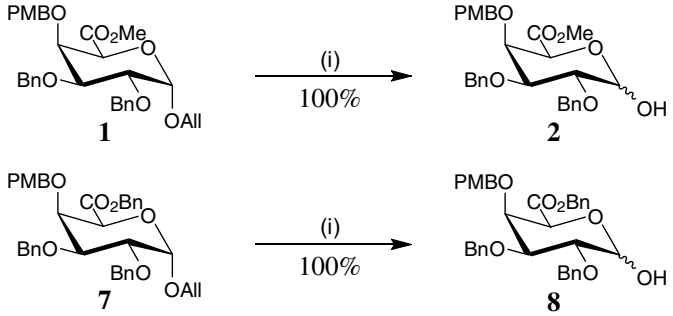
On the other hand, the use of organomagnesians[12] is precluded for uronic acids derivatives, due to the alkaline hydrolysis of the ester function, and the acidity of the H-5 that could lead to epimerisation. A reported method[13] for allyl cleavage, using $NaBH_4$ and I_2, was tested (entry 9), but no reaction was observed. Finally, a direct allyl deprotection of **4** was assayed in the presence of $ZnCl_2$, $Pd(PPh_3)_4$ and Bu_3SnH[14] (entry 10). Here a reductive medium is used, and as expected, the oxidized product was not detected; however, the reaction did not go to completion.

Two-step procedures involve an initial isomerisation of allyl into prop-1-enyl glycoside, followed by a smooth cleavage of the last one by mercuric compounds.[15] The isomerisation can be performed by a diversity of reagents. The most often employed is *t*BuOK,[16] but this strong base is not adapted for uronic acid derivatives. Milder methods employing iridium[17] or rhodium[18] complex have been described. In both cases, catalytic amounts of reagents are used. Cycloocta-1,5-dienebis[methyldiphenylphosphine]iridium hexafluorophosphate was tested (entry 11), but after 16 h no evolution was observed. Finally, compound **4** was reacted with DABCO and $(Ph_3P)_3RhCl$ (entry 12). After 48 h only the propenyl compound was present. Moreover, the reaction can be easily followed by the colour change of the reaction mixture, from red to colourless. The crude propenyl was treated with HgO and $HgCl_2$ in acetone–water, leading to the desired compound **6** within 25 min. These conditions were applied to galacturonic acid derivatives **1** and **7** (Scheme 3). After the isomerisation in the presence of rhodium catalyst (16 h) and mercuric-assisted propenyl cleavage, compounds **2** and **8** were obtained in 100% yield.

Compounds **2** and **8** could then be conveniently activated as glycosyl donors as, for example, trichloroacetimidates or bromides. Considering the nature of the intermediate prop-1-enyl glycoside (I), the use of deprotection conditions to obtain disaccharides directly was investigated. In the cleavage step, the anomeric hydroxyl group is regenerated with water in the presence of mercuric ions, and water might be replaced by a

Table 1. Deallylation of compound **4**

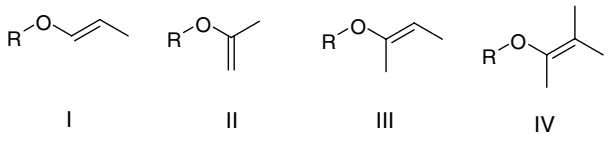
Entry	Reaction conditions	Conversion (%)	**5/6** Ratio
1	$PdCl_2$, AcONa, AcOH, H_2O	91	38/62
2	$Pd(OAc)_2$, AcONa, AcOH, H_2O	90	42/58
3	$PdCl_2$, MeOH	83	41/59
4	$Pd(OAc)_2$, MeOH	88	33/67
5	$PdCl_2$, CH_2Cl_2	0	No reaction
6	$PdCl_2$, *t*BuOH	0	No reaction
7	$PdCl_2$, $BuNH_2$	0	No reaction
8	$PdCl_2$, CuI, DMF, H_2O, O_2	92	39/61
9	$NaBH_4$, I_2	0	No reaction
10	$Pd(PPh_3)_4$, $ZnCl_2$, Bu_3SnH, THF	55	100/0
11	(i) Ir complex; (ii) HgO, $HgCl_2$	0	No reaction
12	(i) Rh complex, DABCO; (ii) HgO, $HgCl_2$	100	100/0



Scheme 3. Reagents and conditions: (i) (a) $(Ph_3P)_3RhCl$, DABCO, EtOH, PhMe, H_2O, 16 h; (b) $HgCl_2$, HgO, acetone, H_2O, 1 h 30 min.

suitable protected sugar derivative having a free hydroxyl group.

Substituted isopropenyl glycosides (II–IV) have been previously activated in the presence of electrophiles as glycosylation donors.[19] NIS/triflic acid, TMSOTf and $BF_3{\cdot}Et_2O$ in acetonitrile are the systems typically used for activationl; however, only a few examples gave both very good yields and α/β selectivity.



Therefore, compound **7** was isomerised as before in the presence of Wilkinson catalyst, then the propenyl compound was quickly purified by flash chromatography and reacted in the conditions of propenyl cleavage ($HgCl_2$, HgO, acetone) with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose. Unfortunately, no glycosylation was observed, and the addition of TMSOTf did not make any difference. In view of these disappointing results, the mechanistic pathway of the reaction was further investigated.

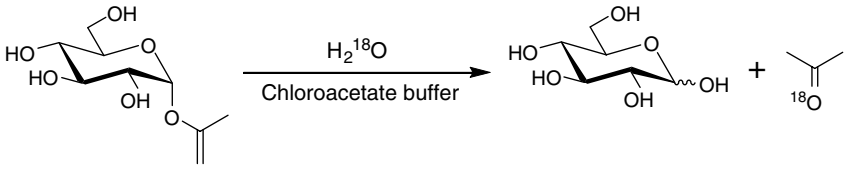
Chenault and Chafin[20] obtained spectroscopic evidence on the mechanism of acid hydrolysis of isopropenyl glucopyranosides. Using [^{18}O]water, they could prove unequivocally that during hydrolysis, the vinyl ether C–O bond is cleaved, and not the glycosidic C–O bond (Scheme 4).

Therefore, the reaction of prop-1-enyl glycoside **7′** was performed in the same conditions (HgO, $HgCl_2$, acetone) but using 95% $^{18}OH_2$. The possible mechanisms are depicted in Scheme 5. If, as previously expected, the water molecule attacks the anomeric carbon atom (route 1), the isotopic labelling will be found at the anomeric position, and this is the only mechanism allowing a glycosylation reaction to be envisaged.[21] On the other hand, the nucleophile attack may occur at the sp^2 carbon atom linked to the oxygen (route 2) or at the other unsaturated carbon atom (route 3).

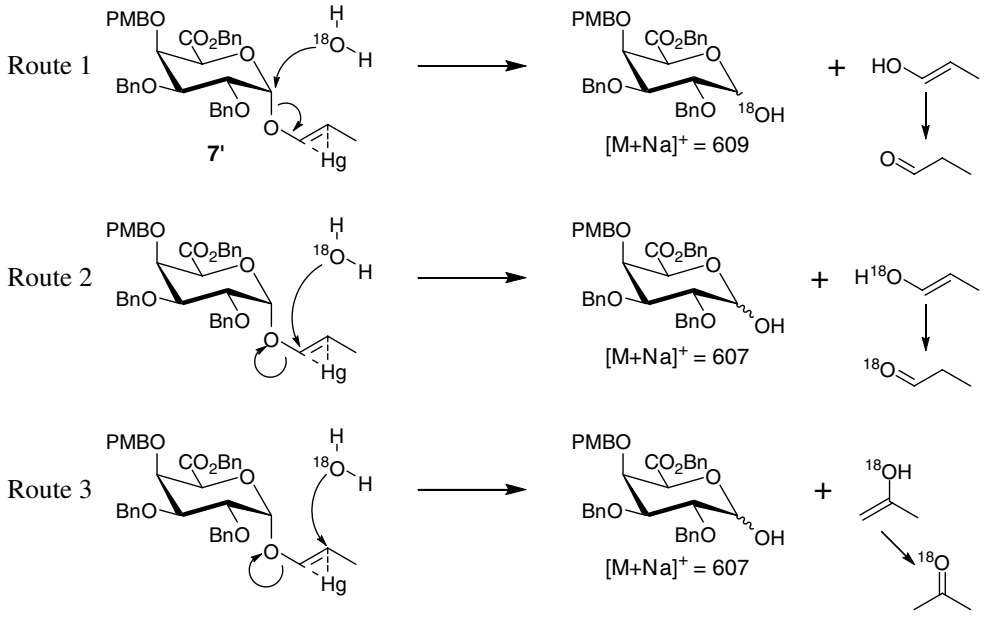
ESI-MS analysis of the reaction mixture indicated that no ^{18}O was incorporated at the anomeric position of the galacturonic acid derivative, only a peak at *m*/*z* 607 (and not at *m*/*z* 609) was detected. This finding suggested that the glycosidic C–O bond is not cleaved during the reaction, the mechanism must follow either route 2 or route 3.

In the case of isopropenyl glycosides, it is clear that the nucleophile goes to the carbon atom linked to the oxygen which can better stabilize the positive charge. However, in our case this position is not substituted, and the possibility of introduction of the water molecule at the β-position must also be considered. As shown in Scheme 5, the incorporation of [^{18}O]water at C-1 of the alkenyl moiety would result in the formation of [^{18}O]propanal, while the final product of C-2 attack would be [^{18}O]acetone.

To prove unequivocally the position of water incorporation, the solvent was distilled from the reaction mixture and analyzed by NMR spectroscopy. Changes in ^{13}C NMR chemical shifts upon isotopic substitution with ^{18}O have been well documented.[18,22] In the ^{13}C NMR spectrum (solvent $CDCl_3$) of the distilled solvent, no signal arising from propanal was detected. A resonance at δ 207.43 corresponding to acetone C=O was observed, and a second resonance shifted 0.05 ppm upfield appeared at δ 207.38, and can be assigned to the [^{18}O]acetone pro-



Scheme 4.



Scheme 5.

duced by propenyl cleavage. As a consequence, the water molecule attacks the C-2 of the alkenyl moiety.

In conclusion, allyl deprotection of galacturonic acid derivatives was performed by a two-step procedure involving rhodium-assisted double bond isomerisation followed by mercuric-catalyzed prop-1-enyl cleavage. Furthermore, during the second step the vinyl ether C–O bond is cleaved, and not the glycosidic C–O bond. The lack of substitution at C-1 of the alkenyl moiety makes the β carbon atom more electrophilic.

1. Experimental

1.1. General methods

Melting points were determined on a Büchi 535. Optical rotations were measured with a Perkin Elmer Model 343 polarimeter using a sodium lamp at 20 °C. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. High-resolution electrospray mass spectra in the positive ion mode were obtained on a Q-TOF Ultima Global hybrid quadrupole/time-of-flight instrument (Waters-Micromass, Manchester, UK), equipped with a pneumatically-assisted electrospray (Z-spray) ion source and an additional sprayer (Lock Spray) for the reference compound. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AC 300 spectrometer.

1.2. Methyl (allyl 2,3-di-*O*-benzyl-4-*O*-*p*-methoxybenzyl-α-D-galactopyranosid)uronate (1)

To a solution of allyl 2,3-di-*O*-benzyl-4-*O*-*p*-methoxybenzyl-α-D-galactopyranosiduronic acid[23] (2.63 g, 4.92 mmol), $KHCO_3$ (3.10 g, 31.0 mmol) and Bu_4NI (182 mg, 0.49 mmol) in anhydrous DMF (180 mL), MeI (1.62 mL, 26.1 mmol) was added under argon. After stirring for 14 h at rt, the solvent was evaporated under diminished pressure. The residue was dissolved in Et_2O, and the solution was washed with brine. The organic layer was separated, dried (Na_2SO_4), filtered and the solvent evaporated. Flash chromatography on silica gel (7:3 hexane–EtOAc) afforded pure **1** (2.46 g, 91% yield) as a colourless gum: $[\alpha]_D^{29}$ +34 (*c* 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.47–7.28 (m, 10H, H_{Ar}–Bn), 7.20 (d, 2H, J_0 8.6 Hz, H_{Ar}–PMB), 6.81 (d, 2H, J_0 8.6 Hz, H_{Ar}–PMB), 5.93 (dddd, 1H, $J_{2',3'trans}$ 17.0 Hz, $J_{2',3'cis}$ 10.4 Hz, $J_{1'a,2'}$ 5.2 Hz, $J_{1'b,2'}$ 6.4 Hz, H-2′), 5.34 (dq, 1H, $J_{2',3'trans}$ 17.0 Hz, J_{gem} 1.5 Hz, $J_{1',3'a}$ 1.5 Hz, H-3′a), 5.23 (ddt, 1H, $J_{2',3'cis}$ 10.4 Hz, J_{gem} 1.5 Hz, $J_{1',3'b}$ 1.2 Hz, H-3′b), 5.02 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 4.89 (d, 1H, J_{gem} 11.7 Hz, C*H*HPh), 4.88 (d, 1H, J_{gem} 11.4 Hz, C*H*HPMP), 4.84 (d, 1H, J_{gem} 12.1 Hz, C*H*HPh), 4.78 (d, 1H, J_{gem} 11.7 Hz, CH*H*Ph), 4.68 (d, 1H, J_{gem} 12.1 Hz, CH*H*Ph), 4.56 (d, 1H, J_{gem} 11.4 Hz, CH*H*PMP), 4.45 (d, 1H, $J_{4,5}$ 1.5 Hz, H-5), 4.32 (dd, 1H, $J_{3,4}$ 2.7 Hz, $J_{4,5}$ 1.5 Hz, H-4), 4.19 (dddd, 1H, J_{gem} 13.0 Hz, $J_{1'a,2'}$ 5.2 Hz, $J_{1'a,3'a}$ 1.5 Hz, $J_{1'a,3'b}$ 1.2 Hz, H-1′a), 4.13 (dd, 1H, $J_{1,2}$ 3.4 Hz, $J_{2,3}$ 10.4 Hz, H-2), 4.06 (dddd, 1H, J_{gem} 13.0 Hz, $J_{1'b,2'}$ 6.4 Hz, $J_{1'b,3'a}$ 1.5 Hz, $J_{1'b,3'b}$ 1.2 Hz, H-1′b), 4.05 (dd, 1H, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 2.7 Hz, H-3), 3.80 (s, 3H, Ar–OCH_3), 3.68 (s, 3H, CO_2CH_3). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.2 (C-6), 159.0 (C_i–OMe), 138.5 (C_i–CH_2Bn), 138.3 (C_i–CH_2Bn), 133.5 (C-2′), 130.4 (C_i–CH_2PMB), 129.5 (C_{Ar}–PMB), 128.3–127.3 (C_{Ar}–Bn), 118.1 (C-3′), 113.4 (C_{Ar}–PMB), 96.6 (C-1), 78.2 (C-3), 76.1 (C-4), 75.7 (C-2), 74.2 (*C*H_2PMP), 73.4 (*C*H_2Ph), 73.3

(CH_2Ph), 70.8 (C-5), 68.7 (C-1′), 55.1 (Ar–OCH_3), 52.1 (CO_2CH_3); HRESIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{32}H_{36}O_8Na$, 571.2308; found, 571.2330.

1.3. Methyl 2,3-di-*O*-benzyl-4-*O*-*p*-methoxybenzyl-D-galactopyranuronate (2)

A solution of compound **1** (1.01 g, 1.82 mmol), $(Ph_3P)_3RhCl$ (138 mg, 0.15 mmol) and DABCO (42 mg, 0.36 mmol) in 7:3:1 EtOH–toluene–H_2O (110 mL) was stirred at reflux for 16 h. After filtration through Celite and solvent evaporation, the crude propenyl derivative was dissolved in 9:1 acetone–H_2O (25 mL). $HgCl_2$ (1.52 g, 5.52 mmol) and red HgO (40 mg, 0.18 mmol) were added. After stirring for 1 h 30 min at rt, acetone was evaporated and the residue was dissolved in EtOAc, and the solution washed with brine. The organic layer was separated, dried (Na_2SO_4), filtered and the solvent evaporated. Flash chromatography on silica gel (2:3 hexane–EtOAc) afforded pure **2** (936 mg, 100% yield, α/β ratio 64:36) as a colourless gum. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.86 (m, 10H, H_{Ar}–Bn), 7.19 (m, 2H, H_{Ar}–PMB), 6.88 (m, 2H, H_{Ar}–PMB), 5.44 (br s, 0.6H, H-1α), 5.00 (d, 0.4H, J_{gem} 10.6 Hz, C*H*HAr), 4.88 (d, 0.6H, J_{gem} 11.5 Hz, C*H*HAr), 4.86 (d, 0.8H, J_{gem} 11.6 Hz, C*H*HAr), 4.85 (d, 0.7H, J_{gem} 12.4 Hz, C*H*HAr), 4.83 (d, 0.8H, J_{gem} 10.6 Hz, CH*H*Ar), 4.78 (d, 0.5H, J_{gem} 11.6 Hz, CH*H*Ar), 4.76 (d, 0.4H, J_{gem} 12.2 Hz, CH_2Ar), 4.75 (d, 0.6H, J_{gem} 12.4 Hz, CH*H*Ar), 4.69 (d, 0.4H, $J_{1\beta,2\beta}$ 6.9 Hz, H-1β), 4.66 (br s, 0.6H, H-5α), 4.60 (d, 1.2H, J_{gem} 11.5 Hz, CH*H*Ar), 4.36 (m, 0.6H, H-4α), 4.26 (m, 0.4H, H-4β), 4.13 (dd, 0.6H, $J_{1\alpha,2\alpha}$ 3.3 Hz, $J_{2\alpha,3\alpha}$ 9.9 Hz, H-2α), 4.07 (m, 0.4H, H-5β), 4.05 (d, 0.6H, $J_{2\alpha,3\alpha}$ 9.9 Hz, $J_{3\alpha,4\alpha}$ 2.3 Hz, H-3α), 3.95 (br s, 1H, OH), 3.86 (d, 0.4H, $J_{1\beta,2\beta}$ 6.9 Hz, $J_{2\beta,3\beta}$ 9.5 Hz, H-2β), 3.82 (s, 1.8H, OCH_3PMB α), 3.80 (s, 1.2H, OCH_3PMB β), 3.69 (s, 1.8H, CO_2CH_3 β), 3.68 (s, 1.2H, CO_2CH_3 α), 3.61 (dd, 0.4H, $J_{2\beta,3\beta}$ 9.5 Hz, $J_{3\beta,4\beta}$ 2.8 Hz, H-3β). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.4 (C-6α), 168.7 (C-6β), 159.0 (C_i–OMe), 138.3 and 138.0 (C_i–CH_2Bn), 130.3 and 130.0 (C_i–CH_2PMB), 129.7 and 129.6 (C_{Ar}–PMB), 128.3–127.4 (C_{Ar}–Bn), 113.1 (C_{Ar}–PMB), 97.5 (C-1β), 91.8 (C-1α), 81.2 (C-3β), 80.0 (C-2β), 77.9 (C-3α), 75.7 (C-2α), 75.5 (C-4α), 74.9 (CH_2Ph), 74.5 (C-4β), 74.1 (CH_2Ph), 74.0 (CH_2Ph), 73.8 (C-5β), 73.3 (CH_2Ph), 72.9 (CH_2Ph), 70.5 (C-5α), 55.1 (OCH_3PMB), 52.3 (CO_2CH_3 β), 52.1 (CO_2CH_3 α); HRESIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{29}H_{32}O_8Na$, 531.1995; found, 531.1991.

1.4. Benzyl (allyl 2,3-di-*O*-benzyl-4-*O*-*p*-methoxybenzyl-α-D-galactopyranosid)uronate (7)

Compound **7** was prepared from the corresponding galacturonic acid (2.15 g, 4.02 mmol) as for compound **1**, but replacing MeI by benzyl bromide. Flash chromatography on silica gel (9:1 hexane–EtOAc) afforded pure **7** (2.31 g, 92% yield) as a colourless gum: $[\alpha]_D^{29}$ +17 (*c* 0.25, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.45–7.28 (m, 15H, H_{Ar}–Bn), 7.15 (d, 2H, J_0 8.7 Hz, H_{Ar}–PMB), 6.73 (d, 2H, J_0 8.7 Hz, H_{Ar}–PMB), 5.94 (dddd, 1H, $J_{2',3'trans}$ 17.0 Hz, $J_{2',3'cis}$ 10.3 Hz, $J_{1'a,2'}$ 5.2 Hz, $J_{1'b,2'}$ 6.5 Hz, H-2′), 5.35 (dq, 1H, $J_{2',3'trans}$ 17.0 Hz, J_{gem} 1.5 Hz, $J_{1',3'a}$ 1.5 Hz, H-3′a), 5.24 (ddt, 1H, $J_{2',3'cis}$ 10.3 Hz, J_{gem} 1.5 Hz, $J_{1',3'b}$ 1.1 Hz, H-3′b), 5.20 (d, 1H, J_{gem} 12.1 Hz, CO_2CHHPh), 5.05 (d, 1H, $J_{1,2}$ 3.3 Hz, H-1), 5.02 (d, 1H, J_{gem} 12.1 Hz, CO_2CHHPh), 4.90 (d, 1H, J_{gem} 11.7 Hz, C*H*HPh), 4.85 (d, 1H, J_{gem} 11.2 Hz, C*H*HPMP), 4.84 (d, 1H, J_{gem} 12.0 Hz, C*H*HPh), 4.77 (d, 1H, J_{gem} 11.7 Hz, CH*H*Ph), 4.69 (d, 1H, J_{gem} 12.0 Hz, CH*H*Ph), 4.50 (d, 1H, $J_{4,5}$ 1.6 Hz, H-5), 4.48 (d, 1H, J_{gem} 11.2 Hz, CH*H*PMP), 4.33 (dd, 1H, $J_{3,4}$ 2.7 Hz, $J_{4,5}$ 1.6 Hz, H-4), 4.21 (dddd, 1H, J_{gem} 13.1 Hz, $J_{1'a,2'}$ 5.2 Hz, $J_{1'a,3'a}$ 1.5 Hz, $J_{1'a,3'b}$ 1.1 Hz, H-1′a), 4.16 (dd, 1H, $J_{1,2}$ 3.4 Hz, $J_{2,3}$ 10.2 Hz, H-2), 4.08 (dddd, 1H, J_{gem} 13.1 Hz, $J_{1'b,2'}$ 6.5 Hz, $J_{1'b,3'a}$ 1.5 Hz, $J_{1'b,3'b}$ 1.1 Hz, H-1′b), 4.06 (dd, 1H, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 2.7 Hz, H-3), 3.79 (s, 3H, OMe). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 168.4 (C-6), 158.9 (C_i–OMe), 138.5 (C_i–CH_2Bn), 138.3 (C_i–CH_2Bn), 135.1 (C_i–CH_2CO_2Bn), 133.5 (C-2′), 130.5 (C_i–CH_2PMB), 129.3 (C_{Ar}–PMB), 128.4–127.3 (C_{Ar}–Bn), 118.1 (C-3′), 113.4 (C_{Ar}–PMB), 96.6 (C-1), 78.3 (C-3), 76.0 (C-4), 75.7 (C-2), 74.0 (CH_2PMP), 73.4 (CH_2Ph), 73.3 (CH_2Ph), 70.7 (C-5), 68.7 (C-1′), 66.8 (CO_2CH_2Ph), 55.1 (OMe); HRESIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{38}H_{40}O_8Na$, 647.2621; found, 647.2618.

1.5. Benzyl 2,3-di-*O*-benzyl-4-*O*-*p*-methoxybenzyl-D-galactopyranuronate (8)

Compound **8** was prepared from **7** (957 mg, 1.53 mmol) as for compound **2**. Flash chromatography on silica gel (2:3 hexane–EtOAc) afforded pure **8** (896 mg, 100% yield, α/β ratio 78:22) as a colourless gum. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.36 (m, 15H, H_{Ar}–Bn), 7.15 (m, 2H, H_{Ar}–PMB), 6.82 (m, 2H, H_{Ar}–PMB), 5.46 (dd, 0.8H, $J_{1\alpha,OH}$ 3.0 Hz, $J_{1\alpha,2\alpha}$ 3.4 Hz, H-1α), 5.21 (d, 0.8H, J_{gem} 12.1 Hz, CO_2CHHPh α), 5.03 (d, 0.8H, J_{gem} 12.1 Hz, CO_2CHHPh α), 4.99 (d, 0.8H, J_{gem} 11.9 Hz, C*H*HAr α), 4.98 (d, 0.2H, J_{gem} 10.9 Hz, CO_2CHHPh β), 4.93 (d, 0.2H, J_{gem} 10.9 Hz, CO_2CHHPh β), 4.86 (d, 0.2H, J_{gem} 10.0 Hz, C*H*HAr β), 4.84 (d, 0.8H, J_{gem} 12.8 Hz, C*H*HAr α), 4.83 (d, 0.8H, J_{gem} 11.0 Hz, C*H*HAr α), 4.82 (d, 0.8H, J_{gem} 11.9 Hz, CH*H*Ar α), 4.80 (d, 0.2H, J_{gem} 10.6 Hz, C*H*HAr β), 4.79 (d, 0.2H, J_{gem} 10.0 Hz, CH*H*Ar β), 4.73 (d, 0.8H, J_{gem} 12.8 Hz, CH*H*Ar α), 4.72 (d, 0.2H, J_{gem} 11.8 Hz, C*H*HAr β), 4.68 (d, 1H, $J_{4\alpha,5\alpha}$ 1.4 Hz, H-1β-5α), 4.63 (d, 0.2H, J_{gem} 11.8 Hz, CH*H*Ar β), 4.50 (d, 0.8H, J_{gem} 11.0 Hz, CH*H*Ar α), 4.46 (d, 0.2H, J_{gem} 10.6 Hz, CH*H*Ar β),

4.35 (dd, 0.8H, $J_{3\alpha,4\alpha}$ 2.6 Hz, $J_{4\alpha,5\alpha}$ 1.4 Hz, H-4α), 4.29 (m, 0.2H, OH β), 4.25 (m, 0.2H, H-4β), 4.13 (dd, 0.8H, $J_{1\alpha,2\alpha}$ 3.4 Hz, $J_{2\alpha,3\alpha}$ 9.9 Hz, H-2α), 4.09 (d, 0.2H, $J_{4\beta,5\beta}$ 1.2 Hz, H-5β), 4.04 (dd, 0.8H, $J_{2\alpha,3\alpha}$ 9.9 Hz, $J_{3\alpha,4\alpha}$ 2.6 Hz, H-3α), 3.87 (dd, 0.2H, $J_{1\beta,2\beta}$ 7.5 Hz, $J_{2\beta,3\beta}$ 9.5 Hz, H-2β), 3.80 (s, 2.4H, OCH_3PMB α), 3.78 (s, 0.6H, OCH_3PMB β), 3.69 (d, 0.8H, $J_{1\alpha,OH}$ 3.0 Hz, OH α), 3.61 (dd, 0.2H, $J_{2\beta,3\beta}$ 9.5 Hz, $J_{3\beta,4\beta}$ 2.9 Hz, H-3β). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 168.6 (C-6α), 167.8 (C-6β), 158.8 (C_i–OMe), 138.1 (C_i–CH_2Bn), 137.8 (C_i–CH_2Bn), 134.8 (C_i–CH_2CO_2Bn), 130.2 (C_i–CH_2PMB α), 129.9 (C_i–CH_2PMB β), 129.3 (C_{Ar}–PMB β), 129.2 (C_{Ar}–PMB α), 128.4–127.2 (C_{Ar}–Bn), 113.3 (C_{Ar}–PMB), 97.4 (C-1β), 91.7 (C-1α), 81.1 (C-3β), 79.8 (C-2β), 77.8 (C-3α), 75.6 (C-2α), 75.3 (C-4α), 74.7 (CH_2Ph), 74.3 (C-4β), 73.8–73.7 (C-5β, 2 × CH_2Ph), 73.2 (CH_2Ph), 72.8 (CH_2Ph), 70.4 (C-5α), 69.5 (CH_2Ph), 66.9 (CO_2CH_2Ph β), 66.8 (CO_2CH_2Ph α), 54.9 (OCH_3PMB); HRESIMS (*m*/*z*): $[M+Na]^+$ calcd for $C_{35}H_{36}O_8Na$, 607.2307; found, 607.2302.

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