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Carbohydrate-derived iminium salt organocatalysts for the asymmetric epoxidation of alkenes

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ABSTRACT

A new family of carbohydrate-based dihydroisoquinolinium salts has been prepared and tested for potential as asymmetric catalysts for the epoxidation of unfunctionalized alkene substrates, providing up to 57% ee in the product epoxides.

1. Introduction

The importance of non-racemic chiral epoxides lies in their versatility as building blocks for the synthesis of enantiomerically enriched compounds of value such as biologically active molecules.[1] Although there exist several catalytic procedures by which chiral epoxides can be synthesised in high enantiomeric purity,[2] the enantioselective oxidation of prochiral alkenes remains the usual synthetic route to such compounds. As a consequence of the potential of asymmetric epoxidation and the value of chiral epoxides, the process has received considerable attention over many years from a number of research groups. Despite all this activity, however, to date there is still no general method in existence for the catalytic asymmetric epoxidation of all classes of alkenes. Nonetheless, several highly effective methods are known for the epoxidation of various classes of alkenes whose corresponding epoxides are obtained in good to excellent enantioselectivities, and great advances in such procedures have been made in recent years.

There are several well-known procedures for the catalytic asymmetric epoxidation of simple alkenes where the catalyst used is in the form of a metal–organic ligand complex. Macrocyclic porphyrin ligand complexes of iron(III),[3] manganese(III)[4] and ruthenium(III)[5] are able to effect the asymmetric epoxidation of simple unfunctionalized alkenes, albeit in low to moderate yields. The salen–manganese complexes developed independently by Katsuki[6] and Jacobsen[7] offer vastly improved catalytic systems for the asymmetric epoxidation of prochiral unsaturated *cis*- and trisubstituted aryl alkenes, which are epoxidized with high to excellent enantioselectivities. The most well-known of these metal–ligand systems is probably that reported by Sharpless in 1980 and applicable uniquely to allylic alcohol substrates, which are generally transformed into their corresponding epoxides with very high enantioselectivities indeed (typically >90%).[8]

Despite the high enantioselectivities and relatively low catalyst loadings required in many of the metal–ligand based catalyst systems described, organocatalysts offer a desirable alternative, particularly in terms of economic and environmental considerations. Dioxirane-based catalysts remain the largest group of organic catalysts developed to date with respect to the asymmetric epoxidation of simple and unfunctionalized alkenes. In 1984 Curci reported the first asymmetric epoxidation of an alkene with a chiral ketone catalyst.[9] Since then great advances have been made over the past several years in this area of asymmetric oxidation. Such systems generally use Oxone as the stoichiometric oxidant, where the dioxirane is generated in situ from a chiral ketone in the presence of the substrate. Among the most notable chiral ketones are those reported by Yang,[10] Denmark,[11] Adam[12] and Armstrong.[13] However, the most prominent of these chiral ketone systems to date are the

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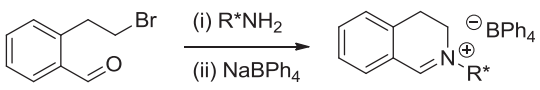
fructose-related ketones developed by Shi, which typically provide high ees for the catalytic asymmetric epoxidation of various substrates and different oxidants.[14] However, as a consequence of catalyst destruction due to competing Baeyer–Villiger side reactions, dioxirane-mediated epoxidations usually require relatively high catalytic loadings of chiral ketone, typically ranging upwards from 20 to 30 mol %. Other sugar-derived ketones have also been used as precursors of dioxiranes for asymmetric epoxidation.[15]

Oxaziridines are nitrogen analogues of dioxiranes, formed by oxidation of the corresponding imines. Like dioxiranes, some are able to transfer an atom of oxygen to an alkene substrate, although reactivity is low. Significant disadvantages of oxaziridine-mediated epoxidations are the relatively long reaction times (3–12 h at 60 °C) and the usual requirement for a stoichiometric amount of reagent,[16] although we[17] and DuBois[18] have reported the catalytic use of oxaziridines. It is believed that the epoxidation process is a concerted one since retention of double bond stereochemistry is observed at the new asymmetric centre(s) created in the process. Because this process is performed under neutral conditions, it is particularly suitable for the oxidation of labile substrates. Davis has reported ees of greater than 90% for the asymmetric epoxidation of α-methylstilbene with his oxaziridine systems, and has shown that they are able to oxidise chiral sulfides to their corresponding chiral sulfoxides with ees of up to 78%.[19]

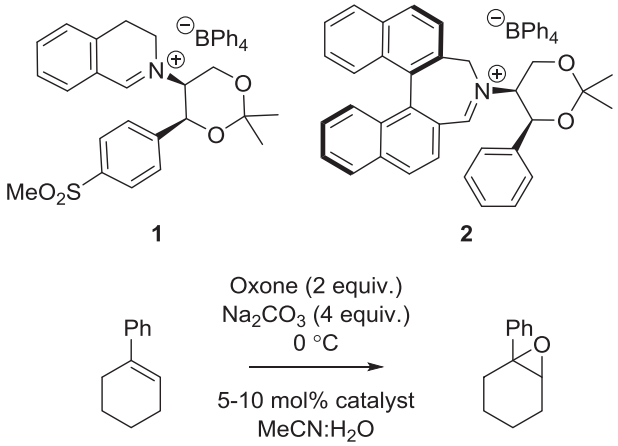
Oxaziridinium salts, which were first reported by Lusinchi in 1976,[20] are the quaternized derivatives of oxaziridines. Usually prepared in situ by the action of oxone on the corresponding iminium salts, they offer advantages over oxaziridines in that they are much more reactive, and are highly effective as catalytic oxidants.[21] Furthermore, because of the positively charged oxaziridinium nitrogen atom, they are more electrophilic than their parent oxaziridines and therefore transfer oxygen to nucleophilic substrates more readily. Unlike some dioxirane-based systems, these catalysts are not prone to Baeyer–Villiger decomposition during epoxidation reactions, but they can suffer from degradation, for example, by aromatisation. Such problems have been effectively circumvented by Bohé by the use of iminium salts with dialkyl-substituted heterocyclic rings.[22] Exocyclic chiral iminium salts have been used in asymmetric epoxidation processes but enantioselectivities observed have been moderate.[23] Amines have also been used in epoxidation processes by us[24] and others.[25]

Our research in this area has been largely focused on fused cyclic iminium salt systems. Over the past several years, we have developed dihydroisoquinolinium salt systems where different exocyclic chiral moieties containing the controlling asymmetric centre(s) have been attached to the iminium nitrogen atom.[26] Such catalysts are readily derived from the condensation of chiral primary amines with 2-(2-bromoethyl)benzaldehyde as shown in Scheme 1. The bromide salts tend to be oils that are difficult to purify by conventional methods, and we have found that anion exchange with sodium tetraphenylborate yields crystalline salts that are easy to handle and purify.



Scheme 1.

Our work has resulted in the discovery of some of the most successful iminium salt catalysts to date, both in terms of enantioselectivity and reactivity, including members of the dihydroisoquinolinium-based family such as **1**. A series of 1,3-dioxane-based catalysts have also been developed where the dihydroisoquinolinium moieties have been replaced by biphenyl and binaphthalene azepinium-fused moieties.[27] In the case of the latter, under the standard aqueous conditions used (Scheme 2), one particular catalyst **2** with catalyst loadings ranging from as little as 0.1–5 mol %, has produced ees ranging from 88 to 91% for the epoxidation of 1-phenylcyclohexene. Different oxidants have also been used under aqueous conditions;[28] we have also developed non-aqueous conditions using tetraphenylphosphonium monoperoxysulfate (TPPP)[29] as the oxidant,[30] and we have used this set of conditions to access several chromene-based natural products in very high enantioselectivities.[31]



Scheme 2.

We reasoned that incorporation of carbohydrate moieties into our iminium salts might improve both the selectivity and reactivity of the catalysts. We report herein the synthesis and development of several novel carbohydrate-derived dihydroisoquinolinium salt catalyst systems and the assessment of their potential as mediators in the asymmetric epoxidation of simple unfunctionalised alkene substrates under aqueous conditions.

1.1. Catalyst design

Our rationale in choosing to develop carbohydrate-derived iminium salts as potential epoxidation catalysts was based on several features: the large number of polar hydroxyl groups, which we considered might help to order the epoxidation transition state complex; the structural diversity available in carbohydrate structures, which would allow tuning and versatility; and the conformational rigidity and well-understood structures, particularly in the case of pyranose monosaccharides. We had also observed good enantioselectivities and excellent reactivity in catalysts such as **1** and **2**, where the stereocontrolling elements are contained in a related six-membered dioxane structure. We further postulated that we might be able to alter significantly the enantioselectivities of these catalysts by changing the protecting groups on their hydroxyl functionalities. Initially we identified a number of glycosylamine derivatives **3**–**8**, shown in Fig. 1, as ideal building blocks for our catalyst synthesis by cyclocondensation with 2-(2-bromoethyl) benzaldehyde.

2. Results and discussion

We began with the synthesis of perbenzylated glucose-, mannose- and galactose-based catalysts, which were accessed from their respective known glycosylamine precursors 1-amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-glucopyranose **3a**, 1-amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-mannopyranose **3b** and 1-amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-galactopyranose **3c**. The synthesis of amines **3a**–**c** started from *O*-methyl-α-D-glucopyranoside,

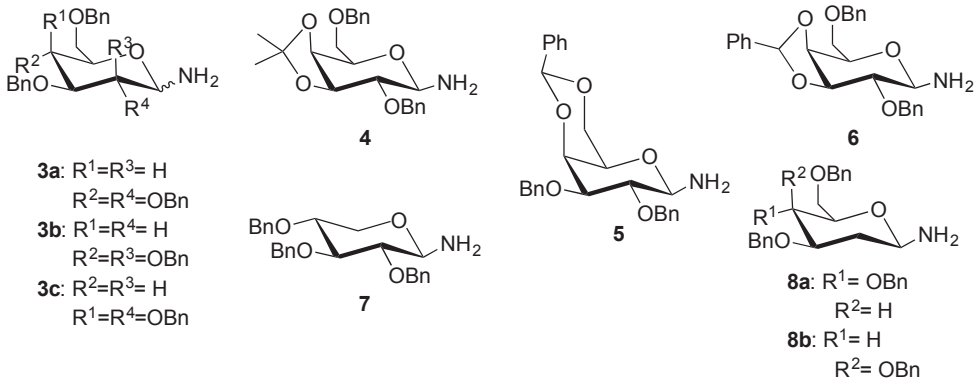
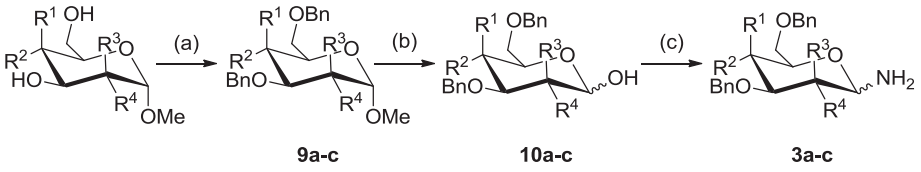


Fig. 1. Target amine precursors for iminium salt catalysts.

O-methyl-α-D-mannopyranoside and *O*-methyl-α-D-galactopyranoside, respectively (Scheme 3, Table 1). Benzylation of the four hydroxyl moieties proceeded in excellent yields, in each case using sodium hydride in DMF (87–96% yield). Removal of the anomeric methoxy moiety with acid led to the corresponding tetrabenzyl pyranoses **9a**–**c** in fair yields (32–41%) as mixtures of anomers (2:1 to 3:1 ratio α/β). Displacement of the anomeric hydroxyl unit was achieved as a two-step one-pot process by conversion of the free hydroxyl group to the corresponding mesylate, which was then displaced by ammonia giving amines **3a**–**c** in moderate yields (52–63%) as mixtures of anomers (1:3 to 1:4 ratio α/β) following a known procedure from Aebisher.[32]

To achieve the synthesis of amine **5**, D-galactose was converted into tetra-acetyl bromide **16** in 94% yield through acetylation of the anomeric hydroxyl group followed by treatment with bromine in the presence of red phosphorus (Scheme 5). Displacement of the bromide in allyl alcohol in the presence of mercuric bromide and mercuric cyanide gave ether **17** in 52% yield. Hydrolysis of the acetate moieties proceeded in 96% yield using methanoate as the base. Formation of the acetal using *para*-toluenesulfonic acid as the catalyst gave 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranose **15** in 60% yield as a mixture of anomers (α/β ratio 2:1). Mesylation followed by displacement using ammonia gave amine **4** in 68% yield as a mixture of anomers (α/β ratio 5:7).



Reagents and conditions: (a) BnCl, NaH, DMF, heat, 3 h; (b) AcOH, 2M HCl, heat, 6 h; (c) (i) Et_3N, MsCl, CH_2Cl_2, –20 °C, 4 h; then (ii) NH_3, –78 °C to r.t., 72 h.

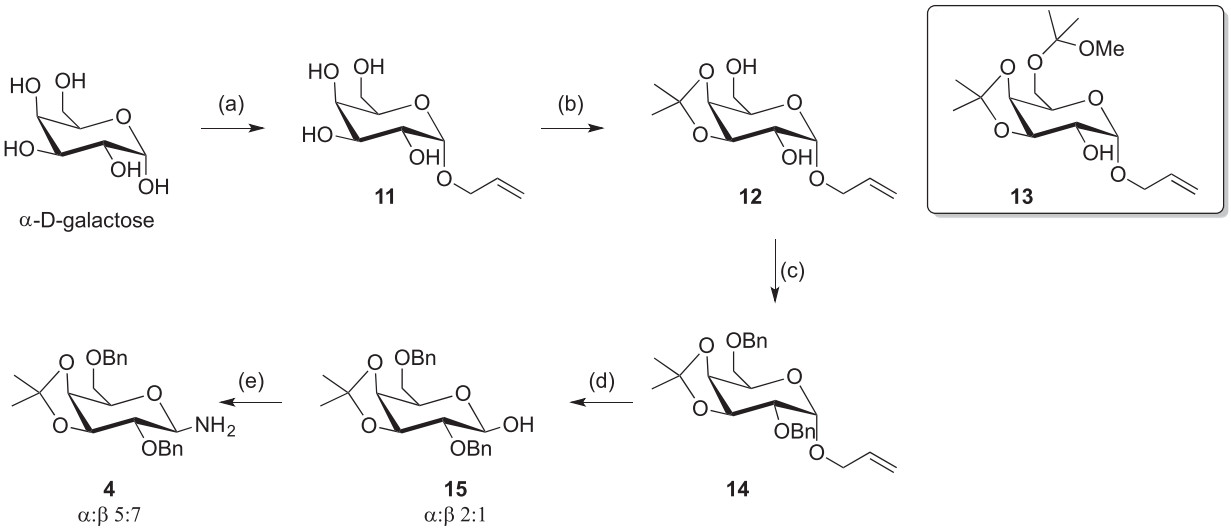
Scheme 3.

Table 1
Synthesis of amines **3a**–**c**

Starting material	Step (a)		Step (b)			Step (c)		
	Compound	Yield (%)	Compound	Yield (%)	α/β	Compound	Yield (%)	α/β
R^1=R^3=H; R^2=R^4=OH	**9a**: R^1=R^3=H; R^2=R^4=OBn	93	**10a**: R^1=R^3=H; R^2=R^4=OBn	37	2:1	**3a**: R^1=R^3=H; R^2=R^4=OBn	63	1:3
R^1=R^4=H; R^2=R^3=OH	**9b**: R^1=R^4=H; R^2=R^3=OBn	87	**10b**: R^1=R^4=H; R^2=R^3=OBn	41	2:1	**3b**: R^1=R^4=H; R^2=R^3=OBn	57	1:4
R^2=R^3=H; R^1=R^4=OH	**9c**: R^2=R^3=H; R^1=R^4=OBn	96	**10c**: R^2=R^3=H; R^1=R^4=OBn	32	3:1	**3c**: R^2=R^3=H; R^1=R^4=OBn	52	1:4

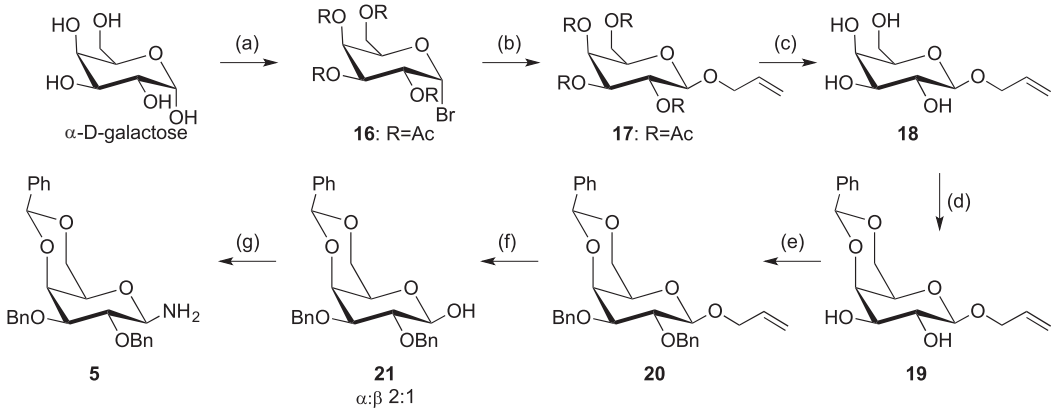
The galactose-derived glycosylamines **4**–**6** and the 5-deoxy derivative **7** were accessed from the corresponding alcohols. Thus, synthesis of amine **4** commenced from D-galactose (Scheme 4). Allyl-α-D-galactoside **11** was prepared using acetyl chloride in allyl alcohol in 26% yield. Our first attempts at the formation of isopropylidene **12** were unsatisfactory as yields lower than 10% were observed. Indeed, literature precedent shows that the preferred product is the 6-*O*-(1-methoxy-1-methyl)ethyl derivative **13**.[33] Addition of triethylamine leads to the formation of triethylammonium tosylate, which acts as a weak acid and allows the selective cleavage of the 6-*O*-(1-methoxy-1-methyl)ethyl group when the solution is heated under reflux. Using this procedure, galactoside **12** was obtained in 67% yield. Benzylation of the remaining hydroxyl moieties proceeded in 71% yield. Isomerisation of the double bond followed by cleavage of the resulting enol ether followed by benzylation of the remaining hydroxyl groups gave compound **20** in 71% yield over the two steps. Wilkinson's catalyst was then used to remove the allyl group. The yield of the reaction was lower than expected as a result of competing formation of the corresponding saturated compound through hydrogenation catalysed by the rhodium complex. Mesylation followed by displacement using ammonia gave amine **5** in 63% yield as a mixture of anomers.

Amines **6** and **5** were prepared using the same initial pathway up to allyl β-D-glycoside **18** (Scheme 6). To obtain amine **6**, glycoside **18** was converted to the corresponding isopropylidene derivative **23** using camphorsulfonic acid as the catalyst in 2,2-dimethoxypropane, followed by benzylation of the remaining hydroxyl groups in 47% yield over the two steps. Removal of the isopropylidene protecting group followed by acetal formation gave two products: the expected '*exo*'-product **25b** as the slower eluting



Reagents and conditions: (a) (i) Allyl alcohol, AcCl, 5 °C to r.t., 26%; (b) (i) $(CH_3)_2C(OMe)_2$, CSA, then (ii) MeOH:H_2O (10:1), reflux, 67%; (c) NaH, BnBr, DMF, 0 °C to r.t., 95%; (d) (i) *t*-BuOK, DMSO, 100 °C then (ii) HgO, $HgCl_2$, MeCN:H_2O (9:1), 63%; (e) (i) Et_3N, MsCl, CH_2Cl_2, –20 °C, 4 h; then (ii) NH_3, –78 °C to r.t., 72 h, 68%.

Scheme 4.



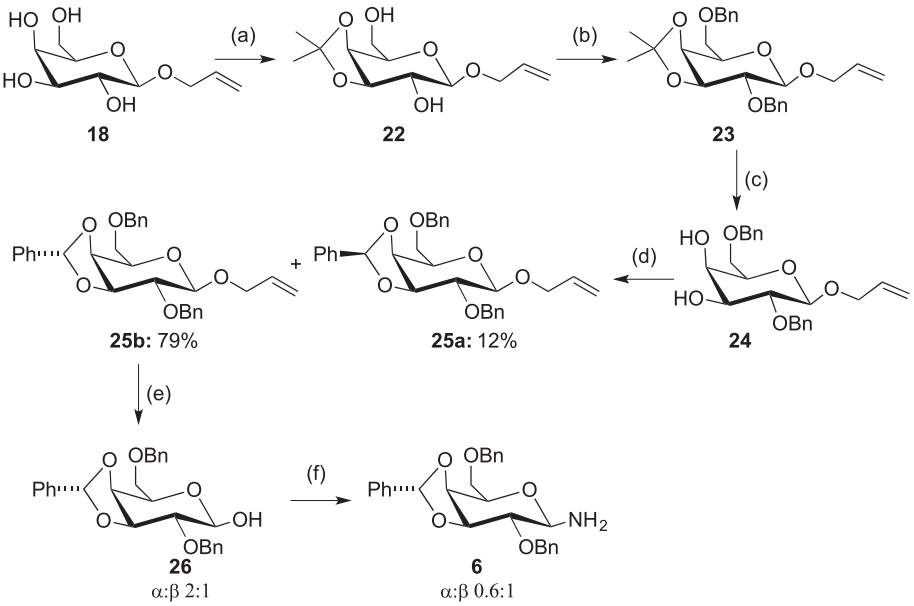
Reagents and conditions: (a) (i) $HClO_3$, Ac_2O, 5 °C to r.t., then (ii) Red phosphorus, Br_2, 94%; (b) Allyl alcohol, HgBr, $HgCN_2$, Drierite, 52%; (c) MeONa, MeOH, 96%; (d) $PhCH(OMe)_2$, *p*-TSA, MeCN, 78%; (e) NaH, BnBr, DMF, 0 °C to r.t., 91%; (f) (i) $RhCl(PPh_3)_3$, DABCO, EtOH (95%), 80 °C, then (ii) I_2, pyridine, THF:H_2O (8:2), 51%; (g) (i) Et_3N, MsCl, CH_2Cl_2, –20 °C, 4 h; then (ii) NH_3, –78 °C to r.t., 72 h, 63%.

Scheme 5.

isomer in 79% yield and the corresponding '*endo*'-product **25a** in 12% yield. Confirmation of the configuration of epimer **25a** was obtained through single crystal X-ray analysis (Fig. 2). Treatment with mercuric chloride after isomerisation of the double bond led to decomposition of **25b**. Cleavage of the enol ether moiety was achieved under mild conditions using Wilkinson's catalyst in 57% yield as a mixture of anomers (α/β ratio 2:1). The corresponding amine **6** was obtained through in situ displacement of the mesylate by ammonia in 63% yield as a mixture of anomers (α/β ratio 3:5).

The synthesis of amine **7** began from D-xylose (Scheme 7). Acetylation of D-xylose produced the corresponding tetra-acetylated β-xylopyranose **27** in 94% yield. Displacement of the anomeric acetate using thiophenol and boron trifluoride etherate gave thioglycoside **28** in 87% yield. Removal of the remaining acetate using sodium methanoate led to the formation of phenyl 1-thio-β-D-xylopyranoside **29** in 86% yield. Benzylation gave tribenzylated thioglycoside **30** in 67% yield as a mixture of anomers (α/β ratio 1:2). Hydrolysis of the thioglycoside using NBS and aqueous sodium carbonate gave tribenzyl-xylose **31** in a 72% yield as a mixture of anomers (α/β ratio 1:2). Xylose **31** was converted into the corresponding mesylate followed by displacement of the mesylate moiety using ammonia to give the desired amine **7** in 62% yield as a mixture of anomers (α/β ratio 1:2).

Amines **8a** and **8b** were prepared from 3,4,6-tri-*O*-benzyl-D-galactal **32a** and 3,4,6-tri-*O*-benzyl-D-glucal **32b**, respectively. Enol ether hydration of **32a** and 32**b** led to the formation of 3,4,6-tri-*O*-



Reagents and conditions: (a) $(CH_3)_2C(OMe)_2$, CSA, 66%; (b) NaH, BnBr, DMF, 0 °C to r.t., 71%; (c) MeOH: 1M HCl (7:1), 81%; (d) $PhCH(OMe)_2$, *p*-TSA, MeCN; (e) (i) $RhCl(PPh_3)_3$, DABCO, EtOH (95%), 80 °C, then (ii) I_2, pyridine, THF:H_2O (8:2), 57%; (f) (i) Et_3N, MsCl, CH_2Cl_2, –20 °C, 4 h; then (ii) NH_3, –78 °C to r.t., 72 h, 63%.

Scheme 6.

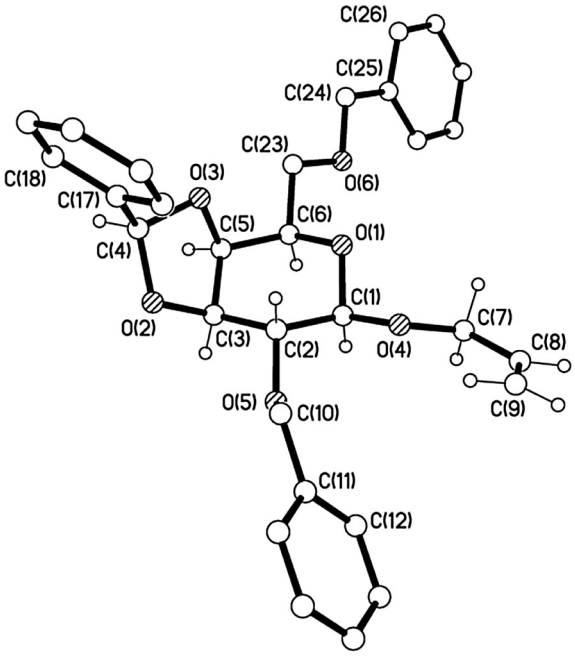


Fig. 2. Single crystal X-ray analysis of **25a**.

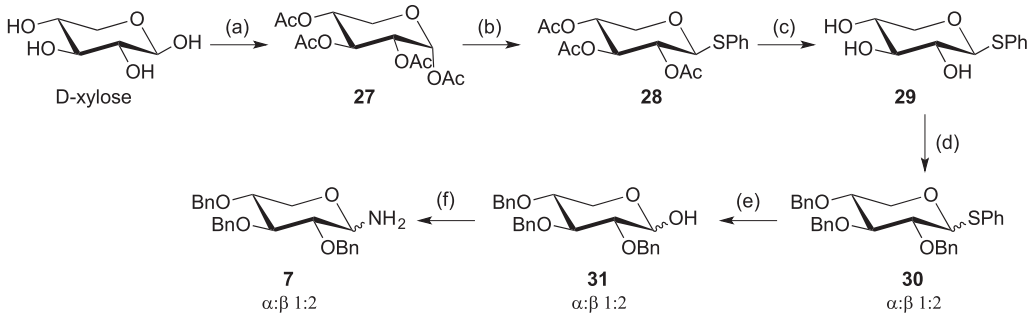
benzyl-2-deoxy-D-galactopyranose **33a** and the corresponding glucopyranose **33b**, in 83 and 90% yields, respectively. Our attempts to synthesise the 2-deoxy-glycosylamines **8a** and **8b** by mesylation and ammonolysis of sugars **33a** and **33b** were unsuccessful as conversions were very low, even after several days. Another possible route involved the formation of azides followed by hydrogenolysis to give the corresponding amines. Conversion of the anomeric hydroxyl groups to the corresponding azides using bromine, sodium azide and triphenylphosphine gave **34a** and **34b** in 43% and 47% yields, respectively. The order of addition of the reagent is critical: if bromine was added first, azide **34b** was obtained in 21% yield, while slow addition of bromine to the mixture led to a moderate improvement (33%). Glycosyl bromide derivative **35** was formed in situ and displacement of the bromide led to the desired azide. However, the bromide derivative is unstable and decomposes readily; hence, our best results were obtained when sodium azide was present in the mixture to displace the bromide as it is produced. Hydrogenation of the azides led to the production of the glycosylamines **8a** and **8b** in 91% and 93% yields, respectively (Scheme 8, Table 2).

With all the desired amine precursors in our hands, the preparation of the catalysts was achieved using 2-(2-bromoethyl)benzaldehyde in ethanol followed by anion exchange using sodium tetraphenylborate, according to our usual procedure (Scheme 9, Table 3).

The synthesis of iminium salts derived from amines **8a** and **8b** was unsuccessful; no iminium signal was observed using ^1H NMR spectroscopic analysis of the reaction mixture, and no crystalline material was recovered from the crude reaction mixture after counter-ion exchange. Single crystal X-ray structure determination of the iminium salt **38**, derived from glycosylamine **5**, was carried out; the structure is shown in Fig. 3.

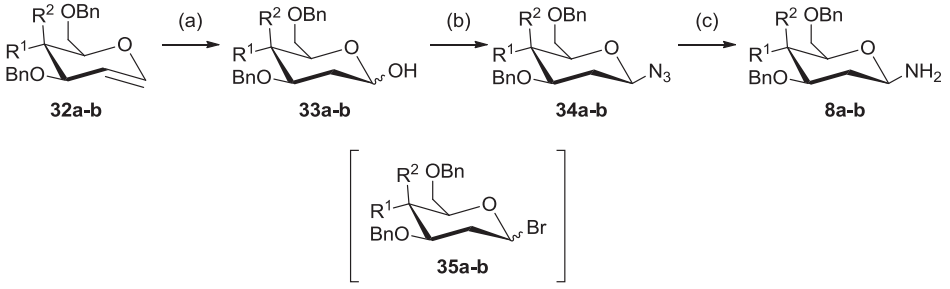
With this series of iminium salts in hand, we next tested their potential as catalysts for asymmetric epoxidation using as test substrates 1-phenylcyclohexene, *trans*-methylstilbene and triphenylethylene (Table 4).

Our results suggest that the spatial arrangement of the benzylated hydroxyl substituents on the pyranose ring may has a marked effect on the magnitude of the induced enantioselectivities of the corresponding epoxide products. Thus, in the case of the mannose-derived catalyst **36b**, with an axial benzyl ether α to the anomeric carbon, there is little or no enantioselectivity observed in the formation of the corresponding epoxides of the test substrates. In sharp contrast, the galactose-derived catalyst **36c**, with an equatorial benzyl ether α to the anomeric carbon, proved to be the best



Reagents and conditions: (a) DMAP, Ac_2O, pyridine, 94%; (b) $BF_3{\cdot}OEt_2$, PhSH, CH_2Cl_2, 0 °C to r.t., 87%; (c) 0.3M MeONa, MeOH, 86%; (d) NaH, BnBr, DMF, 0 °C to r.t., 67%; (e) (i) NBS, MeCN, –15 °C then (ii) $NaHCO_3$(aq), 72%; (f) (i) Et_3N, MsCl, CH_2Cl_2, –20 °C, 4 h; then (ii) NH_3, –78 °C to r.t., 72 h, 62%.

Scheme 7.

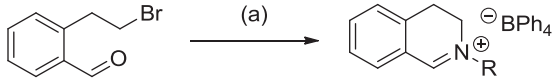


Reagents and conditions: (a) THF:H_2O:0.8M HCl (70:30:1); (b) (i) PPh_3, NaN_3, DMF then (ii) Br_2 0 °C–rt ; (c) H_2, Pd/C, MeOH.

Scheme 8.

Table 2
Synthesis of 2-deoxycarbohydrates

Starting material	Step (a)			Step (b)			Step (c)		
	Compound	Yield (%)	α/β	Compound	Yield (%)	α/β	Compound	Yield (%)	α/β
32a: R^2=H; R^1=OBn	**33a**: R^2=H; R^1=OBn	83	—	**34a**: R^2=H; R^1=OBn	43	1:4	**8a**: R^2=H; R^1=OBn	91	—
32b: R^1=H; R^2=OBn	**33b**: R^1=H; R^2=OBn	90	4:1	**34b**: R^1=H; R^2=OBn	47	1:7	**8b**: R^1=H; R^2=OBn	93	1:3



Reagents and conditions: (a) RNH_2, EtOH, then $NaBPh_4$, MeCN.

Scheme 9.

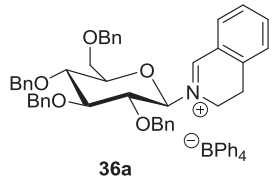
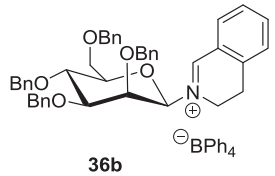
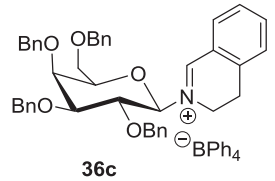
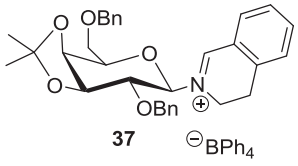
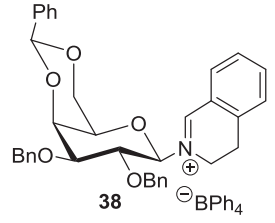
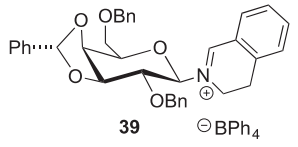
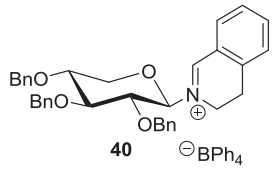
performer of the three towards all of our test substrates, both in terms of conversion and magnitude of induced ee for our least reactive substrate triphenylethylene. This catalyst also provided the highest ee achieved for this series of catalysts, of 57% for the epoxidation of *trans*-methylstilbene. Glucose-derived catalyst **36a**, also with an equatorial benzyl ether α to the anomeric carbon, was also shown to be significantly more enantioselective than the mannose-derived analogue **36b**, but, interestingly, was found to be inferior in this respect to that of the galactose-derived analogue **36c**, with an axial benzyl ether in position C4, which also gave a much higher conversion of 68% in 6 h with the less reactive triphenylethylene substrate.

In order to further investigate the effects of the *O*-benzyl substitution arrangement on enantioselectivity with respect to our glucose-derived catalyst, the similarly related xylose-derived catalyst **40** was prepared and tested. Generally, this catalyst was found to be an inferior mediator in the asymmetric epoxidation of our test substrates compared to its glucose analogue **36a**, giving lower enantioselectivities in the asymmetric epoxidations of 1-phenylcyclohexene and triphenylethylene, but giving the same ee in the epoxidation of *trans*-methylstilbene.

The galactose-derived catalyst **36c** was thus the most effective of our three initial catalysts. We subsequently altered the hydroxyl protecting groups with a view to improving the catalyst properties further; this was achieved by using benzylidene and isopropylidene protecting groups, so altering the protection on two of the hydroxyl positions, C-6 and C-4 or C-4 and C-3: **37** has an isopropylidene group between the hydroxyl groups of C3 and C4, **39** a benzylidene between C3 and C4, and **38** a benzylidene between C4 and C6. This resulted in the preparation of catalysts **37**, **38** and **39** derived from glycosylamines **4**, **5**, and **6**, respectively. Of the three, catalysts **37** and **39**, derived from the glycosylamines **4** and **6**, respectively, were found to induce a rather poor level of asymmetry. Compound **38**, accessed from glycosylamine **5**, induced similar enantioselectivity to catalyst **36c** for the epoxidation of triphenylethylene (57% ee) and the epoxidation of *trans*-methylstilbene (43% ee), but 1-phenylcyclohexene oxide was obtained in a 14% ee (compared to 26% ee for catalyst **36c**).

The absence of a hydroxyl group at C-5 on the pyranose ring of carbohydrate-based dihydroisoquinolinium salt catalysts results in

Table 3
Synthesis of carbohydrate-derived iminium salts **36**–**40**

Amine precursor RNH_2	Iminium salt	Yield (%)	α/β
3a	 **36a**	31	β Only
3b	 **36b**	75	β Only
3c	 **36c**	75	β Only
4	 **37**	43	1:2
5	 **38**	47	β Only
6	 **39**	68	3:8
7	 **40**	35	1:5
8a	Decomposition		
8b	Decomposition		

lower or comparable ees to those with a hydroxyl group based at C-5 (compare catalysts **36a** and **40**, derived from glycosylamines **3a** and **7**).

Where a catalyst based on the galactose configuration has its O-3 and O-4 hydroxyl oxygens protected with a cyclic acetal group (catalysts **37** and **39**, derived from glycosylamines **4** and **6**), there is a significant reduction in the induced enantioselectivity compared with those galactose configurations where O-3 and O-4 oxygens are not protected with such groups (catalysts **36c** and **38**, derived from glycosylamines **3c** and **5**). It therefore appears that for maximum enantioselectivity, the O-3 oxygen should not be part of a cyclic acetal, perhaps for conformational reasons.

It is also evident that a C-2 *O*-benzyl substituent in a catalyst having the D-mannose configuration (catalyst **36b** derived from glycosylamine **3b**) has a profound detrimental effect on the observed induced enantioselectivity.

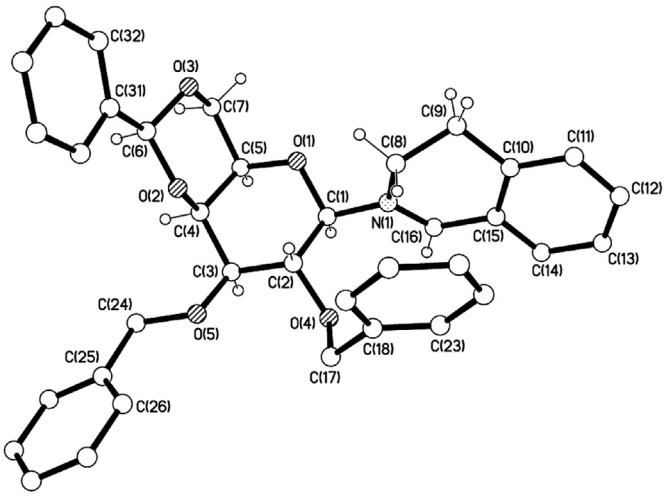
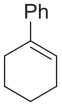


Fig. 3. X-ray crystal structure of the iminium cation **38** derived from glycosylamine precursor **5.**

Table 4
Asymmetric epoxidation of unfuntionalized alkenes mediated by carbohydrate-derived iminium salt catalysts **36**–**40**[a]

Alkene	Catalyst	Time (h)	Yield[b] (%)	ee[c] (%)	Absolute configuration[d]	Conv. (%)
	**36a**	0.75	72	12	(−)-(1*S*,2*S*)	100
	36b	1.25	74	<1	(−)-(1*S*,2*S*)	100
	36c	1.25	74	26	(−)-(1*S*,2*S*)	100
	37	1.0	66	5	(−)-(1*S*,2*S*)	100
	38	1.0	73	14	(−)-(1*S*,2*S*)	100
	39	1.2	71	6	(−)-(1*S*,2*S*)	100
	40	1.0	65	3	(−)-(1*S*,2*S*)	100
	**36a**	1.0	91	18	(−)-(1*S*,2*S*)	100
	36b	1.25	79	1	(−)-(1*S*,2*S*)	100
	36c	1.25	85	57	(−)-(1*S*,2*S*)	100
	37	1.6	66	14	(−)-(1*S*,2*S*)	100
	38	1.0	58	57	(−)-(1*S*,2*S*)	100
	39	1.0	68	9	(−)-(1*S*,2*S*)	100
	40	0.8	67	18	(−)-(1*S*,2*S*)	100
	**36a**	6.0	29	43	(+)-(*S*)	37
	36b	6.0	31	3	(+)-(*S*)	38
	36c	6.0	44	42	(+)-(*S*)	68
	37	6.0	23	13	(+)-(*S*)	26
	38	6.0	40	43	(+)-(*S*)	54
	39	6.0	24	35	(+)-(*S*)	68
	40	6.0	15	34	(+)-(*S*)	27

[a] Conditions: iminium salt (5 mol %), Oxone (2 equiv), Na_2CO_3 (4 equiv), MeCN/H_2O (1:1), 0 °C.
[b] Isolated yields.
[c] Enantiomeric excesses were determined by ^1H NMR spectroscopy in the presence of (+)-Eh(hfc)$_3$. The chiral shift reagent was added until full baseline resolution was observed for the integrated signals.
[d] Absolute configuration of the major enantiomers was determined by comparison of optical rotation with those reported in the literature.

3. Conclusions

Overall, with this family of catalysts, triphenylethylene was, unusually for iminium salt catalysts, the best substrate with regards

to induced enantioselectivity in the epoxide product, but the poorest in terms of conversion of substrate to product, giving at best only 68% conversion with catalyst **36c**. Catalysts **36c** and **38**, derived from galactose, induced the highest ees with the test substrates used in this study. Again unusually for iminium salt catalysed epoxidation, 1-phenylcyclohexene proved to be the poorest substrate in terms of induced enantioselectivity, providing at best just 26% ee with our most effective catalyst.

4. Experimental section

4.1. General experimental methods

Light petroleum (bp 40–60 °C), was distilled from calcium chloride prior to use. Ethyl acetate was distilled over calcium sulfate or chloride. Dichloromethane was distilled over phosphorus pentoxide or calcium hydride. Tetrahydrofuran was distilled under a nitrogen atmosphere from sodium/benzophenone ketyl radical. Triethylamine was stored over sodium hydroxide pellets. Commercially available reagents were used as supplied, without further purification, unless otherwise stated. Air- and moisture-sensitive reactions were carried out using glassware that had been dried overnight in an oven at 240 °C. This was allowed to cool in a desiccator over self-indicating silica gel pellets, under a nitrogen atmosphere. The reactions were carried out under a slight positive pressure of nitrogen. Flash chromatography was carried out using Merck 9385 Kieselgel 60-45 (230–400 mesh). Thin layer chromatography (TLC) was carried out on aluminium plates coated with a silica gel layer 0.25 mm thickness. Compounds were visualised by UV irradiation at a wavelength of 254 nm, or stained by exposure to an ethanolic solution of phosphomolybdic acid (acidified with concentrated sulfuric acid), followed by charring where appropriate. Optical rotation measurements were measured with an Optical Activity-polaAAar 2001 instrument, operating at 589 nm, at the temperature indicated and are reported in units of 10^{-1} deg cm^2 g^{-1}. Melting points were carried out on an Electrothermal-IA 9100 apparatus and are uncorrected. Infra-red absorption spectra were recorded on a Perkin–Elmer FT-IR spectrometer Paragon 2001 instrument in the range of 4000–600 cm^{-1}. Electrospray mass spectrometry was carried out by the EPSRC national Service. ^{1}H NMR spectra were recorded on Bruker AC250 and DPX 400 instruments operating at 250.13 and 400.13 MHz, respectively. ^{13}C NMR spectra were recorded on Bruker DPX 400 instrument operating at 100.62 MHz. Enantiomeric excesses were determined by ^{1}H NMR spectroscopy in the presence of tris((+)-3-(heptafluoropropylhydroxymethylene)camphorato) europium(III), [(+)-Eu(hfc)$_3$], as the chiral shift reagent.

4.2. *General procedure A*: O-benzylation

The starting material (1 equiv) was dissolved in dry DMF (15 mL per 1 g of sugar) under inert atmosphere and the mixture was cooled to 0 °C. Sodium hydride (1.5 equiv per OH group) was added and the mixture stirred for 30 min. Benzyl bromide (1.5 equiv per OH group) was added dropwise over 30 min. The reaction mixture was then allowed to reach room temperature and stirred until completion (ca. 3 h). Methanol was then added (1.0 mL per 1 g of sodium hydride added) and the resulting solution was allowed to stir for a further 10 min. The solvents were removed under reduced pressure and the residue was diluted with water and ethyl acetate. The organic phase was separated, washed with water and brine, dried with magnesium sulfate. The solvents were then removed under reduced pressure and the residue purified using silica gel column chromatography.

4.3. *General procedure B:* removal of the anomeric methoxy group

O-Methyl-2,3,4,6-tetra-*O*-benzyl-pyranoside was dissolved in 80% glacial acetic acid/2 M HCl (10:4; 45 mL per gram of pyranoside) and the reaction mixture was heated under reflux for 11 h. Upon completion, the resulting mixture was allowed to reach room temperature. Dichloromethane (25 mL per gram of pyranoside) was added and the solution was washed using saturated sodium hydrogenocarbonate (2×25 mL per gram of pyranoside). The aqueous layer was extracted using dichloromethane (25 mL per gram of pyranoside). The organic layers were combined, dried using magnesium sulfate and the solvents were removed under reduced pressure. The residue was purified using silica gel column chromatography.

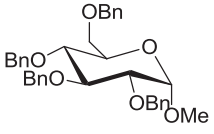
4.4. *General procedure C:* conversion of the anomeric hydroxyl group to a primary amine

The poly-*O*-protected pyranose (1 equiv) was dissolved in dry dichloromethane (5 mL per 1 g of alcohol), triethylamine (2 equiv) was added dropwise under an atmosphere of nitrogen. The resulting solution was then cooled to −20 °C and methanesulfonyl chloride was added (1.8 equiv). After complete mesylation was observed by TLC (ca. 3 h) the reaction mixture was cooled to −78 °C and ammonia gas was condensed into the reaction vessel. The reaction was allowed to reach ambient temperature overnight, after which time the reaction vessel was pressurised with ammonia gas and allowed to stir until complete conversion of mesylate to amine was observed by TLC (ca. 4–5 days). Dichloromethane was removed under reduced pressure and the residue purified by column chromatography.

4.5. *General procedure D:* synthesis of dihydroisoquinolinium salts

A solution of the aminoglygoside in ethanol (10 mL per gram of amine, 1 equiv) was added dropwise via a syringe to 2-(2-bromoethyl)benzaldehyde (1.1 equiv) in a stoppered ice cooled round bottomed flask. After the addition was complete, the reaction mixture was stirred overnight while attaining ambient temperature. Sodium tetraphenylborate (1.1 equiv) in a minimum amount of acetonitrile was added in one portion. After 5 min of stirring, the solvents were removed under reduced pressure and the resulting residue was treated with dichloromethane until the crude product had fully dissolved. After filtration, the dichloromethane was removed from the filtrate under reduced pressure and the resulting gummy residue was washed with ethanol followed by diethyl ether until a solid was obtained.

4.6. *O*-Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside 9a[34]

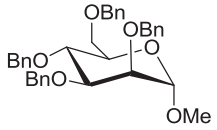


Prepared using general procedure A using *O*-methyl-α-D-glucopyranoside (2.00 g, 10.3 mmol, 1 equiv), sodium hydride (1.48 g, 61.8 mmol, 6 equiv) and benzyl bromide (7.35 mL, 61.8 mmol, 6 equiv). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1:9) gave the desired product as a yellow oil (5.3 g, 93%).

$[\alpha]_D^{24}$ 18.9 (*c* 1.0, $CHCl_3$); lit.: $[\alpha]_D^{21}$ 19.6 (*c* 2.89, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3030, 2905, 1955, 1877, 1813, 1723, 1602, 1495, 1454, 1363, 1198; δ_H (400 MHz, $CDCl_3$) 3.37 (3H, s), 3.50–3.88 (5H, m); 4.00

(1H, d, J=11.7 Hz), 4.92–5.25 (9H, m), 7.18–7.63 (20H, m); δ_C (100 MHz, $CDCl_3$) 55.2, 68.9, 70.5, 73.85, 73.9, 75.5, 76.2, 78.1, 80.2, 82.6, 98.2, 128.05, 128.09, 128.12, 128.15, 128.3, 128.37, 128.43, 128.6, 128.8, 128.85, 128.9, 137.9, 138.1, 138.2, 138.7; HRFABMS: m/z calcd for $[C_{35}H_{38}O_6]^+$: 572.3012; found for $[M]^+$: 572.3009.

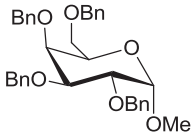
4.7. *O*-Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside 9b[35]



Prepared using general procedure A using *O*-methyl-α-D-mannopyranoside (3.00 g, 15.5 mmol, 1 equiv), sodium hydride (2.23 g, 93.0 mmol, 6 equiv) and benzyl bromide (11.06 mL, 93.0 mmol, 6 equiv). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1:9) gave the desired product as a colourless oil (7.5 g, 87%).

$[\alpha]_D^{23}$ 32.3 (c 1.0, $CHCl_3$); lit.: $[\alpha]_D^{25}$ 31.57 (c 1.38, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3029, 2908, 1955, 1877, 1815, 1729, 1602, 1493, 1453, 1361, 1200; δ_H (400 MHz, $CDCl_3$) 3.31 (3H, s), 3.71–3.81 (4H, m); 3.88 (1H, dd, J=3.1, 9.3 Hz), 3.98 (1H, t, J=9.3 Hz), 4.50 (1H, d, J=10.8 Hz), 4.55 (1H, d, J=12.1 Hz), 4.66 (1H, d, J=12.1 Hz), 4.73 (4H, m), 4.77 (1H, d, J=1.8 Hz), 4.88 (1H, d, J=10.4 Hz), 7.34–7.50 (20H, m); δ_C (100 MHz, $CDCl_3$) 54.7, 69.2, 71.6, 72.1, 72.6, 73.3, 74.5, 74.9, 75.0, 80.2, 98.9, 127.4, 127.51, 127.53, 127.57, 127.7, 127.8, 127.9, 128.27, 128.30, 128.32, 138.28, 138.33, 138.4, 138.5; HRFABMS: m/z calcd for $[C_{35}H_{38}O_6]^+$: 572.3012; found for $[M]^+$: 572.3017.

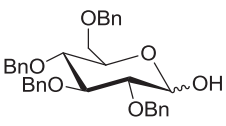
4.8. *O*-Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside 9c[35]



Prepared using general procedure A using *O*-methyl-α-D-galactopyranoside (3.00 g, 15.5 mmol, 1 equiv), sodium hydride (2.23 g, 93.0 mmol, 6 equiv) and benzyl bromide (11.06 mL, 93.0 mmol, 6 equiv). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1:9) gave the desired product as a colourless oil (8.2 g, 96%).

$[\alpha]_D^{23}$ −3.6 (c 1.6, $CHCl_3$); lit.: $[\alpha]_D^{25}$ −3.94 (c 2.03, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3029, 2910, 1952, 1875, 1814, 1722, 1605, 1496, 1454, 1351, 1194; δ_H (400 MHz, $CDCl_3$) 3.48–3.56 (5H, m), 3.57–3.61 (2H, m), 3.81 (1H, dd, J=7.7, 9.7 Hz), 3.89 (1H, d, J=2.9 Hz), 4.27 (1H, dd, J=0.8, 7.7 Hz), 4.39 (1H, d, J=11.8 Hz), 4.44 (1H, d, J=11.8 Hz), 4.61 (1H, d, J=11.6 Hz), 4.67–4.77 (3H, m), 4.89 (1H, d, J=10.9 Hz), 4.94 (1H, d, J=11.7 Hz), 7.21–7.38 (20H, m); δ_C (100 MHz, $CDCl_3$) 57.0, 68.8, 72.9, 73.3, 73.4, 73.5, 74.4, 75.1, 79.6, 82.1, 104.9, 127.48, 127.49, 127.53, 127.8, 127.9, 128.08, 128.12, 128.23, 128.25, 128.3, 128.4, 137.9, 138.5, 138.6, 138.8; HRFABMS: m/z calcd for $[C_{35}H_{38}O_6]^+$: 572.3012; found for $[M]^+$: 572.3009.

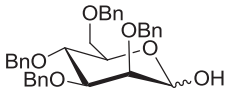
4.9. 2,3,4,6-Tetra-*O*-benzyl-D-glucopyranoside 10a[36]



Prepared using general procedure B using *O*-methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside **9a** (1.7 g, 3.1 mmol). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 3:7) gave the desired product as colourless crystals (0.61 g, 37%) as a mixture of anomers (α/β 2:1 by ^{1}H NMR).

Mp 149–150 °C (lit.: 151–152 °C); $[\alpha]_D^{21}$ 15.6 (c 1.1, $CHCl_3$); lit.: $[\alpha]_D^{25}$ 22 (c 1.0, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3422, 3032, 1454; δ_H (400 MHz, $CDCl_3$) O*H*α and O*H*β exchange, 3.4 (1H, dd≈t, $J_{2,1}$=$J_{2,3}$=8.0 Hz, H-2β), 3.46–3.71 (9H, m, H-6aα, H-6aβ, H-6bα, H-6bβ, 2×C*H*α, 3×C*H*β), 3.99 (1H, dd≈t, J=9.3 Hz, C*H*α), 4.06 (1H, dd, $J_{5,4}$=2.1 Hz, $J_{5,6}$=9.2 Hz, H-5α), 4.44–4.61 (8H, m, 2×PhCH_2α, 4×PhC*H*Hβ), 4.68 (1H, d, J=11.7 Hz, PhC*H*Hα), 4.67 (1H, d, $J_{1,2}$=8.0 Hz, H-1β), 4.74 (1H, d, J=11.5 Hz, PhC*H*Hα), 4.74 (1H, d obscured, J=11.5 Hz, PhC*H*Hβ), 4.76–5.00 (6H, m, 2×PhC*H*Hα, 3×PhC*H*Hβ, H-1α), 7.03–7.61 (40H, m, 20×C*H*α arom., 20×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 68.7 (C-6α), 68.9 (C-6β), 70.2 (*C*Hα), 73.2 (*C*H_2α), 73.5 (*C*H_2α, *C*H_2β), 74.6 (*C*Hβ), 74.8 (*C*H_2β), 75.0 (*C*H_2β), 75.1 (*C*H_2α), 75.3 (*C*H_2β), 75.80 (*C*H_2α), 77.82 (*C*Hα), 77.9 (*C*Hβ), 80.0 (*C*Hα), 81.8 (*C*Hα), 83.1 (*C*Hβ), 84.6 (*C*Hβ), 91.3 (C-1α), 97.5 (C-1β), 127.70, 127.77, 127.80, 127.83, 127.96, 128.03, 128.06, 128.13, 128.2, 128.44, 128.46, 128.48, 128.6, 137.8, 137.9, 137.0, 138.1, 138.17, 138.23, 138.5; HRFABMS: m/z calcd for $[C_{34}H_{36}O_6]^+$: 540.2512; found for $[M]^+$: 540.2514.

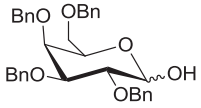
4.10. 2,3,4,6-Tetra-*O*-benzyl-D-mannopyranoside 10b[37]



Prepared using general procedure B using *O*-methyl-2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside **9b** (6.8 g, 12.3 mmol). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1:2) gave the desired product as a colourless oil (2.7 g, 41%) as a mixture of anomers (α/β 2:1 by ^{1}H NMR).

$[\alpha]_D^{22}$ 12.2 (c 0.9, $CHCl_3$); lit.: $[\alpha]_D^{20}$ 11 (c 0.9, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3423, 3029, 1952, 1876, 1808, 1605, 1496, 1363, 1207; δ_H (400 MHz, $CDCl_3$) O*H*α and O*H*β exchange, 3.41–3.46 (1H, m, H-5α), 3.55 (1H, dd, J=2.8 Hz, 9.2 Hz, C*H*α), 3.61–3.73 (4H, m, H-6aα, H-6aβ, H-6bα, H-6bβ), 3.77 (1H, dd, $J_{2,1}$=2.0 Hz, $J_{2,3}$=3.0 Hz, H-2β), 3.79 (1H, dd, $J_{2,1}$=1.4 Hz, $J_{2,3}$=2.9 Hz, *H*-2α), 3.83 (1H, s, H-4β), 3.92 (1H, s, C*H*α), 3.95 (1H, dd, $J_{3,2}$=3.0 Hz, $J_{3,4}$=9.4 Hz, H-3β), 4.00–4.07 (1H, m, H-5β), 4.45–4.57 (3H, m, PhC*H*Hα, PhCH_2β), 4.57–4.63 (5H, m, H-1β, 2×PhCH_2α), 4.65–4.74 (6H, m, PhCH_2α, 2×PhCH_2β), 4.85 (1H, d, J=11.6 Hz, PhC*H*Hβ), 4.87 (1H, d, J=11.0 Hz, PhC*H*Hα), 5.05 (1H, d, J=11.8 Hz, PhC*H*Hβ), 5.22 (1H, d, $J_{1,2}$=1.4 Hz, H-1α), 7.12–7.39 (40H, m, 20×C*H*α arom., 20×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 69.0 (C-6β), 69.6 (C-6α), 71.3 (C-5α), 72.1 (*C*H_2α), 72.56 (*C*H_2β), 72.57 (*C*H_2α), 72.6 (*C*H_2β), 73.2 (*C*H_2α), 73.5 (*C*H_2β), 74.51 (C-4β), 74.55 (*C*H_2β), 74.9 (C-2α), 75.0 (*C*H_2α), 75.1 (C-5β), 75.2 (C-4α), 76.7 (C-2β), 79.7 (C-3α), 82.7 (C-3β), 93.6 (C-1α), 93.7 (C-1β), 127.48, 127.52, 127.57, 127.65, 127.77, 127.83, 127.9, 128.0, 128.1, 128.2, 128.8, 137.9, 138.0, 138.1, 138.32, 138.34, 138.4; HRFABMS: m/z calcd for $[C_{34}H_{36}O_6]^+$: 540.2512; found for $[M]^+$: 540.2520.

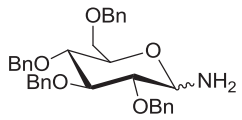
4.11. 2,3,4,6-Tetra-*O*-benzyl-D-galactopyranoside 10c[38]



Prepared using general procedure B using *O*-methyl-2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside **9c** (7.1 g, 12.8 mmol). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 2:3) gave the desired product as a yellow oil (2.1 g, 32%) as a mixture of anomers (α/β 3:1 by ^{1}H NMR).

$[\alpha]_D^{22}$ 19.8 (*c* 1.2, $CHCl_3$); lit.: $[\alpha]_D^{20}$ 20 (*c* 1.5, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3405, 2920, 1951, 1876, 1809, 1737, 1604, 1495, 1453, 1363, 1208; δ_H (400 MHz, $CDCl_3$) O*H*α and O*H*β exchange, 3.40 (1H, dd≈t, $J_{2,1}$=8.0 Hz, H-2β), 3.46–3.71 (9H, m, H-6aα, H-6aβ, H-6bα, H-6bβ, 2×C*H*α, 3×C*H*β), 3.99 (1H, dd≈t, *J*=9.3 Hz, C*H*α), 4.06 (1H, dd, $J_{5,4}$=2.1 Hz, $J_{5,6a}$=$J_{5,6b}$=4.6 Hz, H-5α), 4.41–4.61 (8H, m, 2×PhCH_2α, 2×PhCH_2β), 4.68 (1H, d, *J*=11.7 Hz, PhC*H*Hα), 4.67 (1H, d, $J_{1,2}$=8.0 Hz, H-1β), 4.74 (1H, d, J_I=11.5 Hz, PhC*H*Hα), 4.74 (1H, d, *J*=11.5 Hz, PhC*H*Hβ), 4.76–4.87 (5H, m, PhCH_2α, 3×PhC*H*Hβ), 4.88–5.00 (1H, m, H-1α), 7.03–7.61 (40H, m, 20×C*H*α arom., 20×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 69.0 (C-6β), 69.1 (C-6α), 69.5 (C-5α), 73.0 (CH_2α), 73.49 (CH_2α), 73.50 (CH_2β), 73.52 (CH_2α), 74.57 (CH_2α), 74.60 (CHβ), 74.7 (C-3α), 74.8 (CH_2β), 75.08 (CH_2β), 75.13 (CH_2α), 75.3 (CH_2β), 77.9 (CHβ), 78.7 (C-4α), 83.1 (CHβ), 84.6 (CHβ), 91.9 (C-1α), 97.5 (C-1β), 127.5, 127.60, 127.61, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.29, 128.35, 128.4, 128.5, 137.7, 137.8, 138.2, 138.47, 138.53, 138.60, 138.63, 138.9; HRCIMS: *m*/*z* calcd for $[C_{34}H_{36}O_6+NH_4]^+$ 558.2860; found for $[M+NH_4]^+$: 558.2856.

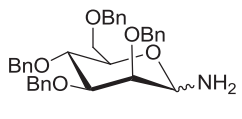
4.12. 1-Amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-glucopyranoside 3a[39]



Prepared using general procedure C using 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoside **10a** (0.50 g, 0.93 mmol). Silica gel column chromatography (eluent: triethylamine/ethyl acetate/light petroleum 1:59:40) gave the desired product as a colourless solid (0.36 g, 63%) as a mixture of anomers (α/β 1:3 by ^{1}H NMR).

Mp 108 °C (lit. 106.5–107.5 °C); $[\alpha]_D^{22}$ 23.1 (*c* 1.4, $CHCl_3$); lit. $[\alpha]_D^{22}$ 17.2 (*c* 0.22, $CHCl_3$); ν_{max} (KBr)/cm^{-1}, 3385, 3335, 3032, 1957, 1884, 1813, 1750, 1454, 1351, 1212; δ_H (400 MHz, $CDCl_3$) 1.9 (4H, br s, N*H*$_2$α, N*H*$_2$β), 3.18 (1H, dd≈t, $J_{2,1}$=$J_{2,3}$=8.6 Hz, H-2β), 3.46 (1H, m, H-5β), 3.53–3.77 (9H, m, 3×C*H*α, 2×C*H*β, H-6aα, H-6aβ, H-6bα, H-6bβ), 3.88 (1H, dd≈t, *J*=9.2 Hz, C*H*α), 4.11 (1H, d, $J_{1,2}$=8.6 Hz, H-1β), 4.45–5.04 (17H, m, 4×PhCH_2α, 4×PhCH_2β, H-1α), 7.12–7.6 (40H, m, 20×C*H*α arom., 20×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 68.7 (C*H*α), 68.9 (C-6α), 69.1 (C-6β), 72.8 (CH_2α), 73.5 (CH_2α), 73.6 (CH_2β), 74.9 (CH_2α), 75.0 (CH_2β), 75.1 (CH_2β), 75.6 (CH_2α), 75.7 (C-5β), 75.8 (CH_2β), 78.2 (CHβ), 79.5 (C*H*α), 80.0 (C*H*α), 81.5 (C*H*α), 83.6 (C-2β), 85.9 (C*H*β), 86.3 (C-1α), 88.2 (C-1β), 127.7, 127.80, 127.82, 127.90, 127.94, 128.0, 128.1, 128.3, 128.4, 128.48, 128.54, 138.0, 138.1, 138.3, 138.4, 138.7, 138.9; HRFABMS: *m*/*z* calcd for $[C_{34}H_{37}NO_5+H]^+$ 540.2750; found for $[M+H]^+$: 540.2757.

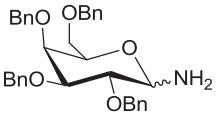
4.13. 1-Amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-mannopyranoside 3b[40]



Prepared using general procedure C using 2,3,4,6-tetra-*O*-benzyl-D-mannopyranoside **10b** (2.0 g, 3.7 mmol). Silica gel column chromatography (eluent: triethylamine/ethyl acetate/light petroleum 1:59:40) gave the desired product as a colourless oil (1.13 g, 57%) as a mixture of anomers (α/β 1:4 by ^{1}H NMR).

$[\alpha]_D^{22}$ 9.6 (*c* 1.0, $CHCl_3$); ν_{max} (neat)/cm^{-1}, 3390, 3330, 3027, 1951, 1875, 1809, 1737, 1605, 1496, 1452, 1361, 1208; δ_H (400 MHz, $CDCl_3$) N*H*$_2$α and N*H*$_2$β exchange, 3.41–3.49 (2H, m, H-6aα, H-6aβ), 3.50–3.66 (5H, m, H-6bα, H-6bβ, 3×C*H*β), 3.82 (1H, dd, $J_{3,2}$=2.9 Hz, $J_{3,4}$=8.9 Hz, H-3α), 3.89 (1H, d, *J*=1.7 Hz, C*H*β), 3.94 (1H, t, *J*=2.6 Hz, C*H*α), 3.99 (1H, dd, *J*=4.3 Hz, *J*=9.0 Hz, C*H*α), 4.06 (1H, dd, *J*=1.1, 7.0 Hz, C*H*β), 4.27–4.34 (1H, m, H-5α), 4.65–4.96 (16H, m, 4×PhCH_2α, 4×PhCH_2β), 5.00 (1H, d, $J_{1,2}$=4.3 Hz, H-1α), 7.12–7.41 (40H, m, 20×C*H*α arom., 20×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) β-anomer 69.2 (C-6), 72.9 (CH_2), 73.6 (CH_2), 73.9 (CH), 74.3 (CH), 74.6 (CH_2), 75.4 (CH_2), 80.7 (CH), 83.5 (CH), 86.6 (C-1), 127.52, 127.56, 127.64, 127.8, 127.9, 128.24, 128.27, 128.32, 128.35, 128.44, 128.47, 137.9, 138.5, 138.6, 138.7; HRFABMS: *m*/*z* calcd for $[C_{34}H_{37}NO_5+H]^+$ 540.2750; found for $[M+H]^+$: 540.2759.

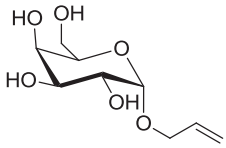
4.14. 1-Amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-galactopyranoside 3c[40]



Prepared using general procedure C using 2,3,4,6-tetra-*O*-benzyl-D-galactopyranoside **10c** (3.0 g, 5.6 mmol). Silica gel column chromatography (eluent: triethylamine/ethyl acetate/light petroleum 1:59:40) gave the desired product as a yellow oil (1.57 g, 52%) as a mixture of anomers (α/β 1:4 by ^{1}H NMR).

$[\alpha]_D^{24}$ 16.3 (*c* 1.0, $CHCl_3$); ν_{max} (neat)/cm^{-1}, 3394, 3030, 1952, 1877, 1810, 1734, 1605, 1496, 1454, 1362, 1208; δ_H (400 MHz, $CDCl_3$) N*H*$_2$α and N*H*$_2$β exchange, 3.60–3.42 (7H, m, H-2α, H-3β, H-4β, H-6aα, H-6aβ, H-6bα, H-6bβ), 3.76 (1H, dd, $J_{2,1}$=7.4 Hz, $J_{2,3}$=8.9 Hz, H-2β), 3.86 (1H, d, *J*=2.9 Hz, H-5β), 3.91 (1H, dd partially obscured, *J*=2.8, 9.7 Hz, H-4α), 3.91–3.96 (1H, m, obscured, H-3α), 4.02 (1H, t, *J*=6.2, Hz, H-5α), 4.38 (1H, d, *J*=11.9 Hz, PhC*H*Hβ), 4.39 (1H, d, *J*=11.9 Hz, PhC*H*Hα), 4.46 (1H, d, *J*=11.9 Hz, PhCH*H*β), 4.47 (1H, d, *J*=11.9 Hz, PhCH*H*α), 4.57 (1H, d, *J*=11.5 Hz, PhC*H*Hα), 4.59 (1H, d, *J*=11.6 Hz, PhC*H*Hβ), 4.64 (1H, d, *J*=7.5 Hz, C*H*β), 4.67–4.84 (7H, m, 2×PhCH_2α, 3×PhCH*H*β), 4.91 (1H, d, *J*=11.0 Hz, PhCH*H*β), 4.92 (1H, d, *J*=11.5 Hz, PhCH*H*α), 4.93 (1H, d, *J*=11.6 Hz, PhCH*H*β), 5.27 (1H, d, *J*=3.6 Hz, H-1α), 7.20–7.42 (40H, m, 20×C*H*α arom., 20×C*H*β arom.); HRFABMS: *m*/*z* calcd for $[C_{34}H_{37}NO_5+H]^+$ 540.2750; found for $[M+H]^+$: 540.2757.

4.15. Allyl-α-D-galactopyranoside 11[41]

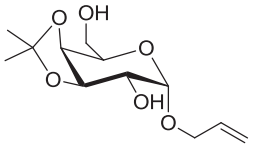


Acetyl chloride (15.0 mL, 210 mmol, 2.5 equiv) was added dropwise to allyl alcohol (190 mL) at 0 °C. Anhydrous α-D-galactose (15.0 g, 83 mmol, 1 equiv) was then introduced. The resulting mixture was heated for 4 h at 70 °C and then at 40 °C for 16 h. The reaction mixture was allowed to reach room temperature and was then carefully neutralised using solid sodium carbonate. The mixture was then filtered on a pad of Celite. The solvents were removed under reduced pressure and the residue was placed on a short silica gel column chromatography (eluent: CH_2Cl_2/MeOH 9:1). The resulting solid was then recrystallised from ethanol to afford the desired product as colourless crystals (4.8 g, 26%).

$[\alpha]_D^{24}$ 178.9 (*c* 1.0, water); lit.: $[\alpha]_D^{25}$ 185 (*c* 6.0, water); ν_{max} (film, KBr)/cm^{-1} 3380, 2942, 1712, 1648, 1504, 1052, 866; δ_H (400 MHz, $(CD_3)_2SO$) 4×−O*H* exchange, 3.40–3.70 (6H, m, CH_2, 4×C*H*), 3.91 (1H, dd, $J_{vicinal}$=5.6 Hz, $J_{geminal}$=14.6 Hz, −OC*H*HCH$_X$=CH$_2$), 4.10 (1H, d, $J_{geminal}$=14.6 Hz, −OCH*H*CH$_X$=CH$_2$), 4.38 (1H, d, $J_{1,2}$=3.2 Hz, H-1), 5.13 (1H, d, $J_{A,X}$=12.2 Hz, −OCH$_2$CH$_X$=C*H*$_A$H$_B$), 5.32 (1H, d, $J_{B,X}$=19.2 Hz, −OCH$_2$CH$_X$=CH$_A$*H*$_B$), 5.75–5.95 (1H, m, −OCH$_2$C*H*$_X$=CH$_2$); δ_C (100 MHz, $(CD_3)_2SO$) 56.4 (CH_2), 67.5 (CH_2), 69.0 (CH), 69.2

(*C*H), 69.9 (*C*H), 71.7 (*C*H), 98.6 (*C*H), 116.5 (*C*H$_2$), 135.4 (−OCH$_2$*C*H$_X$=CH$_2$); HRFABMS: *m*/*z* calcd for [C$_9$H$_{16}$O$_6$+Na]$^+$: 243.0845; found for [M+Na]$^+$: 243.0851.

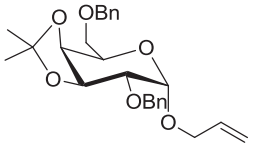
4.16. Allyl-3,4-*O*-isopropylidene-α-D-galactopyranoside 12[42]



Allyl-α-D-galactopyranoside **11** (5.00 g, 22.73 mmol, 1 equiv) and dry camphorsulfonic acid (0.26 g, 1.14, 5 mol %) were dissolved in 2,2-dimethoxypropane under nitrogen atmosphere. The mixture was stirred for 48 h at room temperature. Triethylamine was then added and the mixture was stirred for a further 15 min. The solvents were removed under reduced pressure. The residue was then dissolved in methanol/water (10:1) and the resulting solution was heated under reflux for 7 h. The solvents were then removed under reduced pressure and the residue was purified using silica gel column chromatography (light petroleum/ethyl acetate 2:3) to give the desired product (3.93 g, 67%) as a colourless solid.

Mp 139–140 °C (lit. Mp 138–142 °C); $[\alpha]_D^{22}$ 148.7 (*c* 1.0, CHCl$_3$), lit. $[\alpha]_D^{25}$ 131.5 (*c* 1.0, CHCl$_3$); ν_{max} (neat)/cm^{-1} 3403, 2931, 2359, 2340, 1643, 1074, 1039, 871, 688; δ_H (400 MHz, CDCl$_3$) 2×−O*H* exchange, 1.35 (3H, s, C*H*$_3$), 1.51 (3H, s, C*H*$_3$), 3.75–3.85 (2H, m, H-2, H-6A), 3.90 (1H, dd, $J_{6b,5}$=6.4 Hz, $J_{6b,6a}$=11.8 Hz, H-6b), 4.07–4.10 (2H, m, H-5, −OC*H*HCH$_X$=CH$_2$), 4.23–4.29 (3H, m, 2×C*H*, −OCH*H*CH$_X$=CH$_2$), 4.94 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 5.23 (1H, dd, $J_{A,B}$=1.6 Hz, $J_{A,X}$=10.4 Hz, −OCH$_2$CH$_X$=C*H*$_A$H$_B$), 5.29 (1H, dd, $J_{B,A}$=1.6 Hz, $J_{B,X}$=15.6 Hz, −OCH$_2$CH$_X$=CH$_A$*H*$_B$), 5.85–6.00 (1H, m, −OCH$_2$*C*H$_X$=CH$_2$); δ_C (100 MHz, CDCl$_3$) 25.6 (*C*H$_3$), 27.8 (*C*H$_3$), 62.6 (*C*H$_2$), 68.2 (C-3), 68.3 (*C*H$_2$), 69.6 (C-2), 73.9 (*C*H), 76.3 (*C*H), 96.8 (*C*H), 109.8 (*C*), 117.9 (*C*H$_2$), 135.6 (−OCH$_2$*C*H$_X$=CH$_2$).

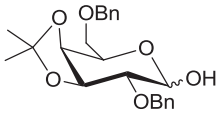
4.17. Allyl-2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranoside 14[42]



Prepared using general procedure A using allyl-3,4-*O*-isopropylidene-α-D-galactopyranoside **12** (3.43 g, 13.2 mmol, 1 equiv), sodium hydride (0.95 g, 39.6 mmol, 3 equiv) and benzyl bromide (4.7 mL, 39.6 mmol, 3 equiv). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1.5:8.5) gave the desired product as a colourless oil (5.38 g, 95%).

$[\alpha]_D^{25}$ 150.6 (*c* 1.1, CHCl$_3$); lit. $[\alpha]_D^{25}$ 215.7 (*c* 0.35, CHCl$_3$); ν_{max} (neat)/cm^{-1} 2916, 2869, 1950, 1870, 1812, 1496, 1028, 237; δ_H (400 MHz, CDCl$_3$) 1.25 (3H, s, CH$_3$), 1.34 (3H, s, CH$_3$), 3.66–3.74 (2H, m, H-6a, H-6b), 4.02 (1H, dd, $J_{vicinal}$=6.4 Hz, $J_{geminal}$=13.2 Hz, −OC*H*HCH$_X$=CH$_2$), 4.15–4.23 (4H, m, H-2, H-4, H-5, −OCH*H*CH$_X$=CH$_2$), 4.36 (1H, dd, $J_{3,4}$=5.2 Hz, $J_{3,2}$=7.6 Hz, H-3), 4.53 and 4.64 (2H, 2d, *J*=12.0 Hz, PhC*H*$_2$), 4.70 and 4.79 (2H, 2d, *J*=12.8 Hz, PhC*H*$_2$), 4.85 (1H, d, $J_{1,2}$=4.0 Hz, H-1), 5.21 (1H, dd obscured, −OCH$_2$CH$_X$=C*H*$_A$H$_B$), 5.32 (1H, dd obscured, −OCH$_2$CH$_X$=CH$_A$*H*$_B$), 5.87–5.97 (1H, m, −CH$_2$*C*H$_X$=CH$_2$), 7.25–7.38 (10H, m, 10×C*H* arom.); δ_C (100 MHz, CDCl$_3$) 25.4 (*C*H$_3$CO), 28.1 (*C*H$_3$CO), 65.3 (*C*H), 66.7 (*C*H$_2$), 69.5 (C-6), 73.2 (*C*H$_2$), 73.3 (*C*H$_2$), 73.7 (*C*H), 75.9 (C-3), 76.3 (C-2), 95.8 (C-1), 105.1 (*C* quat.), 117.2 (*C*H$_2$), 127.49, 127.56, 128.0, 128.30, 128.33, 128.5, 133.6 (−OCH$_2$*C*H$_X$=CH$_2$), 138.22, 138.24; HRFABMS: *m*/*z* calcd for [C$_{26}$H$_{32}$O$_6$]$^+$: 440.2199; found for [M]$^+$: 440.2194.

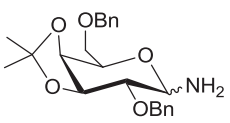
4.18. 2,6-Di-*O*-benzyl-3,4-*O*-isopropylidene-D-galactopyranoside 15[43]



Allyl-2,6-di-*O*-benzyl-3,4-isopropylidene-α-D-galactopyranoside **14** (3.9 g, 9.1 mmol, 1 equiv) was dissolved in anhydrous dimethyl sulfoxide (50 mL) under a nitrogen atmosphere. Potassium *tert*-butoxide (2.03 g, 18.2 mmol, 2 equiv) was added under a blanket of nitrogen. The resulting solution was heated at 100 °C for 1 h under a nitrogen atmosphere. After this time the reaction mixture was allowed to reach room temperature. Water (100 mL) was added and the resulting mixture was extracted with diethyl ether (3×30 mL). The organic extracts were combined, dried and the solvent removed under reduced pressure. The crude enol ether residue was taken up in a solution of mercuric oxide (7.86 g, 36.4 mmol) in 9:1 acetone/water (60 mL). A solution of mercuric chloride (9.83 g, 36.4 mmol) in 9:1 acetone/water (30 mL) was added and the mixture was left to stir. After 30 min, when the reaction had reached completion according to TLC, the solvents were removed under reduced pressure. The residue was taken up in dichloromethane (30 mL) and the resulting solution was washed with a saturated solution of aqueous potassium bromide followed by water, dried (Na$_2$SO$_4$), filtered and concentrated under reduced pressure. The residue was purified by column chromatography (light petroleum/ethyl acetate 7:3) to afford **15** (2.29 g, 63%) as a colourless solid and a mixture of anomers (α/β 2:1 by ^{1}H NMR).

$[\alpha]_D^{23}$ 17.3 (*c* 1.0, CHCl$_3$); lit. $[\alpha]_D^{20}$ 17 (*c* 1.0, CHCl$_3$)]; ν_{max} (film, CHCl$_3$)/cm^{-1} 3544, 3029, 1942, 1869, 1453, 1029; δ_H (400 MHz, CDCl$_3$) −O*H*α and −O*H*β exchange, 1.31 (6H, s, C*H*$_3$α, C*H*$_3$β), 1.38 (3H, s, C*H*$_3$α), 1.39 (3H, s, C*H*$_3$β), 3.34 (1H, dd, $J_{2,3}$=$J_{2,1}$=6.4 Hz, H-2β), 3.56 (1H, dd, $J_{2,1}$=3.6 Hz, $J_{2,3}$=6.8 Hz, H-2α), 3.62–3.78 (4H, m, H-6aα, H-6aβ, H-6bα, H-6bβ), 3.93–4.01 (1H, m, H-5β), 4.09 (1H, dd, partially obscured, $J_{4,5}$=1.6 Hz, H-4β), 4.11 (1H, dd, $J_{4,3}$=2.4 Hz, $J_{4,5}$=6.0 Hz, H-4α), 4.16–4.22 (1H, dd≈t, $J_{3,2}$=$J_{3,4}$=6.4 Hz, H-3β), 4.38–4.44 (2H, m, H-3α, H-5α), 4.48–4.80 (9H, m, 2×PhC*H*$_2$α, 2×PhC*H*$_2$β, H-1β), 5.21 (1H, d, $J_{1,2}$=4.0 Hz, H-1α), 7.23–7.51 (20H, m, 10×C*H*α arom., 10×PhCHβ arom.); δ_C (100 MHz, CDCl$_3$) 25.7 (*C*H$_3$β), 26.5 (*C*H$_3$α), 26.9 (*C*H$_3$β), 28.0 (*C*H$_3$α), 67.1 (C-4α), 67.5 (C-3α), 70.0 (C-6β), 70.1 (C-6α), 72.1 (C-5β), 73.0 (*C*H$_2$α), 73.6 (*C*H$_2$β), 73.8 (*C*H$_2$α), 73.9 (*C*H$_2$β), 74.2 (C-4β), 75.3 (C-5α), 76.2 (C-2α), 78.5 (C-3β), 79.9 (C-2β), 91.2 (C-1α), 96.5 (C-1β), 109.8 (*C*α), 110.0 (*C*β), 127.66, 127.72, 127.8, 127.9, 128.0, 128.1, 128.3, 128.36, 128.40, 128.43, 129.0, 137.7, 137.9, 138.0; HRFABMS: *m*/*z* calcd for [C$_{23}$H$_{18}$O$_6$+H]$^+$: 401.1965; found for [M+H]$^+$: 401.1954.

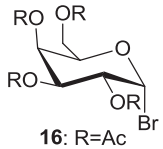
4.19. 1-Amino-2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-D-galactopyranose 4



Prepared using general procedure C using 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-D-galactopyranose **15** (1.50 g, 3.75 mmol). Silica gel column chromatography (eluent: triethylamine/ethyl acetate/light petroleum 1:59:40) gave the desired product **4** as a colourless oil (1.02 g, 68%) as a mixture of anomers (α/β 1:1.4 by ^{1}H NMR).

$[\alpha]_D^{22}$ −167.9 (*c* 1.0, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3395, 3330, 2931, 1878, 1811, 1496, 1318, 1243, 698; δ_H (400 MHz, $CDCl_3$) −N$H_2\alpha$ and −N$H_2\beta$ exchange, 1.32 (3H, s, C$H_3\beta$), 1.33 (3H, s, C$H_3\alpha$), 1.43 (3H, s, C$H_3\alpha$), 1.44 (3H, s, C$H_3\beta$), 3.27 (1H, dd, $J_{2,1}$=$J_{2,3}$=6.8 Hz, H-2α), 3.57–3.81 (5H, m, H-2β, H-6aα, H-6bα, H-6aβ, H-6bβ), 3.91–4.00 (1H, m, H-5α), 4.13–4.25 (4H, m, H-1β, H-3α, H-4α, H-4β), 4.31–4.42 (2H, m, H-3β, H-5β), 4.50–4.87 (9H, m, 2×PhC$H_2\beta$, 2×PhC$H_2\alpha$, H-1α), 7.24–7.39 (10H, m, 10×C$H_2\alpha$ arom., 10×$CH_2\beta$ arom.); δ_C (100 MHz, $CDCl_3$) 25.1 (C$H_3\beta$), 26.6 (C$H_3\alpha$), 27.0 (C$H_3\beta$), 27.8 (C$H_3\alpha$), 67.7 (C-3β), 69.7 (C-6α), 70.1 (C-6β), 72.4 (C-5α), 72.8 (C$H_2\alpha$), 73.0 (C-4β), 73.1 (C-5β), 73.2 (C$H_2\beta$), 73.4 (C$H_2\beta$), 73.6 (C$H_2\alpha$), 74.1 (C-4α), 76.4 (C-2β), 78.1 (C-1β), 79.9 (C-2α), 80.0 (C-3α), 84.7 (C-1α), 109.4 (Cβ), 109.8 (Cα), 127.6, 127.7, 127.77, 127.79, 127.85, 127.9, 128.2, 128.30, 128.32, 128.39, 128.42, 128.5, 137.8, 138.0, 138.2; HRFABMS: *m*/*z* calcd for $[C_{23}H_{19}O_5N+H]^+$: 400.2124; found for $[M+H]^+$: 400.2117.

4.20. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide 16[44]

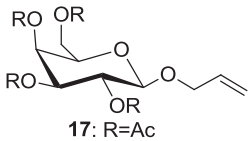


16: R=Ac

Perchloric acid (1.3 mL, 60%) was added dropwise with stirring to ice-cold acetic anhydride (200 mL). The resulting solution was allowed to reach room temperature. After this period, anhydrous α-D-galactose **57** (50 g, 278 mmol, 1 equiv) was added to the stirred mixture at such a rate so that the temperature was maintained between 30 and 45 °C. After cooling to 20 °C, red phosphorus (15 g, 484 mmol, 1.7 equiv) was introduced followed by bromine (30 mL, 586 mmol, 2.1 equiv) at such a rate so that the temperature was maintained below 30 °C. Water (18 mL) was next added over 30 min while the temperature was maintained below 25 °C throughout the addition. After the addition was complete, the mixture was allowed to stir for 2 h. After this time dichloromethane (125 mL) was added. The resulting mixture was filtered through Celite and the filtrate was poured onto ice-cold water (70 mL) and extracted with dichloromethane (3×50 mL). The combined organic extracts were washed with aqueous sodium carbonate, dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was recrystallised from diethyl ether/hexane to afford 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide **16** (107 g, 94%) as a colourless solid.

Mp 85 °C (lit. mp 84–86 °C); $[\alpha]_D^{23}$ 214.3 (*c* 1.3, $CHCl_3$); lit. $[\alpha]_D^{25}$ 210 (*c* 1.0, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 2960, 1749, 1432, 1372, 1222, 913, 600; δ_H (400 MHz, $CDCl_3$) 2.02 (3H, s, CH_3CO), 2.07 (3H, s, CH_3CO), 2.12 (3H, s, CH_3CO), 2.16 (3H, s, CH_3CO), 4.11 (1H, dd $J_{6a,5}$=6.4 Hz, $J_{6a,6b}$=11.4 Hz, H-6a), 4.20 (1H, dd $J_{6b,5}$=6.4 Hz, $J_{6b,6a}$=11.4 Hz, H-6b), 4.49 (1H, t, *J*=3.2 Hz, H-5), 5.05 (1H, dd, $J_{2,1}$=4.0 Hz, $J_{2,3}$=10.4 Hz, H-2), 5.24 (1H, d, $J_{4,5}$=3.2 Hz, H-4), 5.41 (1H, dd, $J_{3,2}$=10.4 Hz, $J_{3,4}$=5.4 Hz, H-3), 6.71 (1H, d, $J_{1,2}$=4.0 Hz, H-1); δ_C (100 MHz, $CDCl_3$) 20.5 (CH_3CO), 20.57 (CH_3CO), 20.62 (CH_3CO), 20.7 (CH_3CO), 60.8 (C-6), 67.0 (C-4), 67.8 (C-2), 68.0 (C-3), 71.1 (C-5), 88.2 (C-1), 169.7 (CH$_3$CO), 169.9 (CH$_3$CO), 170.0 (CH$_3$CO), 170.3 (CH$_3$CO); HRFABMS: *m*/*z* calcd for $[C_{14}H_{19}O_9Br+H]^+$: 411.0291; found for $[M+H]^+$: 411.0293.

4.21. Allyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside 17[45]

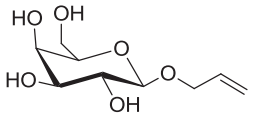


17: R=Ac

A suspension of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide **16** (41.12 g, 100 mmol), Drierite (100 g), mercuric cyanide (13.04 g, 52 mmol) and mercuric bromide (1.44 g, 4 mmol) in dry allyl alcohol (250 mL) was stirred for 7 h at ambient temperature after which time the mixture was concentrated under reduced pressure, diluted with chloroform (400 mL) and filtered. The filtrate was washed successively with 10% aqueous potassium bromide (3×150 mL) and water (2×150 mL), dried ($MgSO_4$) and concentrated in vacuo. The syrupy residue was purified by column chromatography (light petroleum/ethyl acetate, 8:2) to afford **17** (20.2 g, 52%) as a colourless oil.

$[\alpha]_D^{22}$ −6.9 (*c* 1.0, $CHCl_3$); lit. $[\alpha]_D^{25}$ −10.1 (*c* 1.0, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3478, 2981, 2938, 2878, 1749, 1430, 1222, 1055, 955; δ_H (400 MHz, $CDCl_3$) 2.00 (3H, s, CH_3CO), 2.06 (3H, s, CH_3CO), 2.07 (3H, s, CH_3CO), 2.16 (3H, s, CH_3CO), 3.90 (1H, t, $J_{5,4}$=6.8 Hz, H-5), 4.13–4.20 (3H, m, −OC*H*HCH$_X$=CH$_A$H$_B$, H-6a, H-6b), 4.36 (1H, dd, $J_{vicinal}$=5.4 Hz, $J_{geminal}$=13.6 Hz, −OCH*H*CH$_X$=CH$_A$H$_B$), 4.53 (1H, d, $J_{1,2}$=8 Hz, H-1), 5.02 (1H, dd, $J_{3,2}$=10.4 Hz, $J_{3,4}$=3.6 Hz, H-3), 5.18–5.40 (3H, m, H-2, CH_2), 5.40 (1H, d, $J_{4,3}$=H-4), 5.83–5.86 (1H, m); δ_C (100 MHz, $CDCl_3$) 20.6 (CH_3CO), 20.7 (CH_3CO), 20.8 (CH_3CO), 61.3 (C-6), 67.1 (C-4), 68.9 (C-2), 70.0 (CH_2), 70.1 (C-5), 71.0 (C-3), 100.1 (C-1), 117.6 (CH_2), 133.2 (CH), 169.4 (CH$_3$CO), 170.2 (CH$_3$CO), 170.3 (CH$_3$CO), 170.4 (CH$_3$CO); HRFABMS: *m*/*z* calcd for $[C_{17}H_{24}O_{10}-H]^+$ 387.1291; found for $[M-H]^+$ 387.1297.

4.22. Allyl β-D-galactoside 18[46]

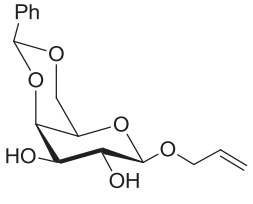


18

A 3 M solution of sodium methoxide was prepared by dissolving sodium methoxide (16.2 g, 300 mmol) in dried freshly distilled methanol (100 mL). Allyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside **17** (20.0 g, 52 mmol) was dissolved in dry methanol (200 mL) followed by the addition of 20 mL of 3 M sodium methoxide solution. The reaction mixture was stirred at room temperature under nitrogen until the reaction had reached completion by TLC (ca. 1 h). After this period Amberlite IR 120 H^+ cation exchange resin was added until neutralisation was effected. The resin was then removed by filtration and the filtrate concentrated under reduced pressure. The resulting residue was purified by triturating and washing with dichloromethane to give the desired compound **18** (11.3 g, 92%).

Mp 100–102 °C (lit. mp 102–103 °C); $[\alpha]_D^{22}$ −12.5 (*c* 1.0, water) [lit. $[\alpha]_D^{27}$ −10.1 (*c* 1.1, water)]; ν_{max} (Nujol)/cm^{-1} 3233, 2854, 1874, 1013, 792, 725; δ_H (400 MHz, $(CD_3)_2SO$) 3.18–3.63 (6H, m, 4×C*H*, H-6a, H-6b), 4.03 (1H, dd, $J_{vicinal}$=5.6 Hz, $J_{geminal}$=13.6 Hz, −OC*H*HCH$_X$=CH$_2$), 4.11 (1H, d, $J_{1,2}$=7.2 Hz, H-1), 4.25 (1H, dd, $J_{vicinal}$=5.6 Hz, $J_{geminal}$=13.6 Hz, −OCH*H*CH$_X$=CH$_2$), 4.38 (1H, d, *J*=4.8 Hz, −O*H*), 4.59 (1H, t, *J*=2.2 Hz, −O*H*), 4.74 (1H, d, *J*=5.2 Hz, −O*H*), 4.94 (1H, d, *J*=4.4 Hz, −O*H*), 5.14 (1H, d, $J_{A,X}$=12.0 Hz, −OCH$_2$CH$_X$=C*H*$_A$H$_B$), 5.34 (1H, d, $J_{B,X}$=18.0 Hz, −OCH$_2$CH$_X$=CH$_A$C*H*$_B$), 5.75–5.95 (1H, m, 1H, d, −OCH$_2$C*H*$_X$=CH$_2$); δ_C (100 MHz, $(CD_3)_2SO$) 60.8 (CH_2), 68.5 (CH), 69.0 (CH_2), 70.9 (CH), 73.7 (CH), 75.5 (CH), 103.0 (C-1), 116.7 (CH_2), 135.4 (−OCH$_2$CH$_X$=CH$_2$); HRFABMS: *m*/*z* calcd for $[C_9H_{16}O_6+Na]^+$: 243.0845; found for $[M+Na]^+$: 243.0847.

4.23. Allyl 4,6-*O*-benzylidene-β-D-galactopyranoside 19[47]

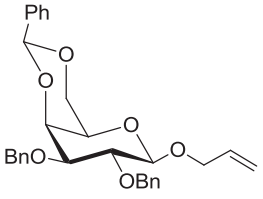


19

Allyl β-D-galactoside **18** (10.0 g, 45 mmol) and *para*-toluenesulfonic acid (0.43 g, 2.27 mmol) were dissolved in wet acetonitrile (60 mL). Benzaldehyde dimethyl acetal (8.9 mL, 59 mmol) was added dropwise and the resulting mixture was allowed to stir for 15 h. After this period the solvent was removed under reduced pressure. The crude residue was purified by column chromatography (dichloromethane/methanol, 9.5:0.5) to afford **19** (10.64 g, 78%) as a colourless solid.

$[\alpha]_D^{20}$ −8 (*c* 1.0, $CHCl_3$), lit. $[\alpha]_D$ −7 (no conditions stated); ν_{max} (film, $CHCl_3$)/cm^{-1} 3474, 2914, 1954, 1874, 1812, 1646, 1496, 1432, 1070, 737, 697; δ_H (400 MHz, $(CD_3)_2SO$) 3.35–3.51 (3H, m, H-2, H-3, H-5), 4.01–4.11 (3H, m, H-4, H-6a, $-OCHHCH_X{=}CH_2$), 4.25 (1H, d, $J_{1,2}$=7.5 Hz, H-1), 4.27–4.31 (2H, m, H-6b, $-OCHHCH_X{=}CH_2$), 4.94 (1H, *J*=5.8 Hz, d, C3−O*H*), 5.08 (1H, dd partially masked, *J*=4.7 Hz, C2−O*H*), 5.16 (1H, dd partially masked, $J_{A,B}$=1.8 Hz, $-OCH_2CH_X{=}CH_AH_B$), 5.36 (1H, dd, $J_{B,A}$=1.8 Hz, $J_{B,X}$=10.5 Hz, $-OCH_2CH_X{=}CH_AH_B$), 5.56 (1H, s, $PhCH(O)_2$), 5.87–5.98 (1H, m, $-OCH_2CH_X{=}CH_2$), 7.33–7.41 (3H, m, 3×C*H* arom.), 7.43–7.49 (2H, m, 2×C*H* arom.); δ_C (100 MHz, $(CD_3)_2SO$) 65.9 (*C*H), 68.6 (CH_2), 68.9 (CH_2), 70.0 (C-2), 71.9 (*C*H), 75.9 (C-4), 99.7 (*C*H), 102.4 (C-1), 116.5 (CH_2), 126.2, 127.9, 128.6, 134.9 ($-OCH_2CH_X{=}CH_2$), 138.7; HRFABMS: *m*/*z* calcd for $[C_{16}H_{20}O_6+H]^+$ 309.1338; found for $[M+H]^+$: 309.1334.

4.24. Allyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside 20[47]

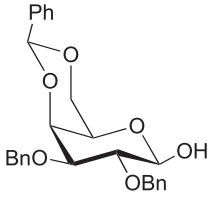


20

Prepared using general procedure A using allyl 4,6-*O*-benzylidene-β-D-galactopyranoside **19** (1.25 g, 4.06 mmol, 1 equiv), sodium hydride (0.29 g, 12.18 mmol, 3 equiv) and benzyl bromide (1.48 mL, 12.18 mmol, 3 equiv). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1:4) gave the desired product **20** (1.80 g, 91%) as a yellow oil.

$[\alpha]_D^{24}$ 31.2 (*c* 1.3, $CHCl_3$); lit. $[\alpha]_D^{29}$ (no conditions stated); ν_{max} (film, $CHCl_3$)/cm^{-1} 3090, 3061, 2907, 2866, 1751, 1646, 1495, 1456, 1383, 1344, 1096, 1046, 735, 697; δ_H (400 MHz, $CDCl_3$) 3.61 (1H, br s, H-4), 3.92–4.35 (7H, m, $-OCH_2CH_X{=}CH_AH_B$, H-2, H-3, H-5, H-6a, H-6b), 4.66 and 4.83 (2H, 2d, *J*=12.0 Hz, $PhCH_2$), 4.73 and 4.83 (2H, 2d, *J*=12.2 Hz, $PhCH_2$), 4.96 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 5.20 (1H, dd, $J_{A,B}$=1.4 Hz, $J_{A,X}$=10.4 Hz, $-OCH_2CH_X{=}CH_AH_B$), 5.30 (1H, dd, $J_{B,X}$=16.0 Hz, $-OCH_2CH_X{=}CH_AH_B$), 5.47 (1H, s, $PhCH(O)_2$), 5.86–5.99 (1H, m, $-OCH_2CH_X{=}CH_2$), 7.17–7.42 (13H, m, 13×C*H* arom.), 7.50–7.56 (2H, m, 2×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 62.7 (C-4), 68.3 (C-6), 69.4 ($-OCH_2CH_X{=}CH_2$), 72.1 (CH_2), 73.4 (CH_2), 74.7 (C-2), 75.3 (C-3), 76.1 (C-5), 96.9 (*C*H), 101.0 (Ph*C*H), 118.0 ($-OCH_2CH_X{=}CH_2$), 127.6, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.8, 133.81 ($-OCH_2CH_X{=}CH_2$), 137.83, 138.6, 138.8; HRFABMS: *m*/*z* calcd for $[C_{30}H_{32}O_6]$: 488.2199; found for $[M]^+$: 488.2207.

4.25. 4,6-*O*-Benzylidene-2,3-di-*O*-benzyl-D-galactopyranose 21[47]

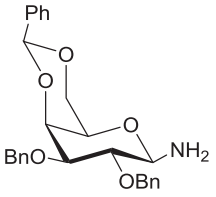


21
α:β 2:1

Allyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside **20** (9.05 g, 18.5 mmol, 1 equiv), 1,4-diazabicyclo[2.2.2]octane (0.41 g, 3.7 mmol, 20 mol %) were dissolved in a mixture of 95% ethanol/toluene/water (ratio 7:3:1, 350 mL). Wilkinson's catalyst (0.86 g, 0.93 mmol, 5 mol %) was then added and the resulting mixture was heated at 80 °C for 17 h. After cooling to room temperature, the solution was concentrated under reduced pressure and the resulting residue dissolved in dichloromethane (50 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford the crude enol ether. The crude enol ether was dissolved in tetrahydrofuran (23 mL). Water (7 mL), pyridine (0.79 mL) and iodine (30.5 g, 120 mmol, 6.5 equiv) were added. The resulting solution was stirred for 10 min at ambient temperature after which time it was cooled to 0 °C and treated with 10% aqueous sodium thiosulfite (50 mL). After 15 min at 0 °C, the solution was extracted with ethyl acetate (3×50 mL) and the combined organic extracts were washed successively with 10% aqueous sodium thiosulfite (2×50 mL) and water (50 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was then purified using silica gel column chromatography (eluent: light petroleum/ethyl acetate 3:2) to give the desired compound **21** (2.45 g, 27%) as a solid and a mixture of anomers (α/β 2:1 by ^1H NMR).

Mp 149–150 °C; $[\alpha]_D^{22}$ 119.3 (*c* 1.0, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 3389, 3085, 1953, 1813, 735, 701; δ_H (400 MHz, $CDCl_3$) α anomer: 3.24 (1H, br s, −O*H*), 3.75 (1H, br s, H-5), 3.91–3.99 (2H, m, H-3, H-6a), 4.03 (1H, dd, $J_{2,1}$=3.6 Hz, $J_{2,3}$=10.0 Hz, H-2), 4.12–4.24 (2H, m, CH, H-6b), 4.66 and 4.87 (2H, 2d, *J*=11.4 Hz, $PhCH_2$), 4.73 and 4.75 (2H, 2d, *J*=12.6 Hz, $PhCH_2$), 5.46 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 5.47 (1H, s, $PhCH(O)_2$), 7.23–7.37 (10H, m, 10×C*H* arom.), 7.38–7.42 (2H, m, 2×C*H* arom.), 7.48–7.56 (2H, m, 2×C*H*).

4.26. 1-Amino-4,6-*O*-benzylidene-2,3-di-*O*-benzyl-β-D-galactopyranose 5

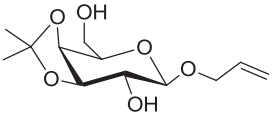


5

Prepared using general procedure C using 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-D-galactopyranose **21** (309 mg, 0.69 mmol). Silica gel column chromatography (eluent: triethylamine/light petroleum/ethyl acetate 1:29:80) gave the desired product **5** as a colourless oil (194 mg, 63%).

$[\alpha]_D^{22}$ −23.6 (*c* 1.3, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 3392, 3031, 2901, 1958, 1890, 1813, 1606, 1169, 1101, 735, 698; δ_H (400 MHz, $CDCl_3$) β anomer: 1.90 (2H, br s, $-NH_2$), 3.30 (1H, s, C*H*), 3.54–3.62 (2H, m, 2×C*H*), 3.97 (1H, dd, $J_{6a,5}$=1.5 Hz, $J_{6a,6b}$=12.0 Hz, H-6a), 4.01–4.19 (3H, m, H-6b, 2×C*H*), 4.75 (2H, m, $PhCH_2$), 4.83 and 4.92 (2H, 2d, *J*=10.8 Hz, $PhCH_2$), 5.48 (1H, s, $PhCH(O)_2$), 7.17–7.42 (13H, m, 13×C*H* arom.), 7.53–7.60 (2H, m, 2×C*H* arom.); HRFABMS: *m*/*z* calcd for $[C_{27}H_{29}O_5N+H]^+$: 448.2124; found for $[M+H]^+$: 448.2131.

4.27. Allyl 3,4-*O*-isopropylidene-β-D-galactopyranoside 22[48]

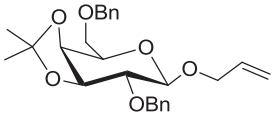


22

Allyl β-D-galactopyranoside **18** (2.17 g, 9.85 mmol, 1 equiv) and *para*-toluenesulfonic acid (187 mg, 0.99 mmol, 10 mol %) were dissolved in *N*,*N*-dimethylformamide (20 mL) and 2,2-dimethoxypropane (40 mL). The resulting solution was then stirred at 40 °C for 5 h or until TLC indicated total consumption of the starting material. After the solution was cooled to room temperature, triethylamine (1.37 mL, 9.85 mmol, 1 equiv) was added and the mixture stirred for 15 min. The mixture was then concentrated to dryness. Toluene (60 mL) was then co-evaporated twice from the residue in order to remove traces of triethylamine. The residue was then dissolved in 10:1 methanol/water (80 mL) and heated under reflux for 30 min until TLC indicated the disappearance of the intermediate product allyl 6-*O*-(2-methoxy-2-propyl)-3,4-*O*-isopropylidene-β-D-galactopyranoside. The reaction mixture was left to cool after which time the solvents were evaporated under reduced pressure. Column chromatography (ethyl acetate/light petroleum 8:2) of the residue afforded the desired product **22** (1.51 g, 59%) as a colourless solid.

Mp 98–99 °C (lit. mp 95.5–97 °C); $[\alpha]_D^{20}$ 5.1 (*c* 0.42, $CHCl_3$), lit. $[\alpha]_D^{22}$ 4.3 (*c* 0.3, $CHCl_3$); ν_{max} (film, $CHCl_3$) 3403, 2931, 2359, 1643, 1381, 1074, 1039, 871, 668; δ_H (400 MHz, $(CD_3)_2SO$) 1.35 (3H, s, CH_3), 1.25 (3H, s, CH_3), 2.60 (1H, br s, 2-OH), 3.09 (1H, br s, 6-OH), 3.58 (1H, t, $J_{2,1}$=$J_{2,3}$=7.8 Hz, H-2), 3.79–3.91 (2H, m, H-5, H-6a), 3.92–4.02 (1H, m, H-6b), 4.07–4.20 (3H, m, H-3, H-4, OC*H*HCH=), 4.26 (1H, d, $J_{1,2}$=7.8 Hz, H-1), 4.39 (1H, ddd, $J_{allylic}$=1.2 Hz, $J_{vicinal}$=5.4 Hz, $J_{geminal}$=11.3 Hz, OCH*H*CH_X=), 5.23 (1H, ddd, $J_{allylic}$=1.3 Hz, $J_{A,B}$=1.5 Hz, $J_{A,X}$=9.2 Hz, CH_X=C*H*$_A$H$_B$), 5.33 (1H, ddd, $J_{allylic}$=1.6 Hz, $J_{A,B}$=1.5 Hz, $J_{B,X}$=17.2 Hz, CH_X=CH_A*H*$_B$), 5.98–5.99 (1H, m, C*H*$_X$=CH_2); δ_C (100 MHz, $(CD_3)_2SO$) 26.3 (CH_3), 31.0 (CH_3), 62.3 (C-6), 69.2 (OCH_2CH=), 73.8 (C-2, C-5), 74.3 (*C*H), 78.9 (*C*H), 101.2 (C-1), 110.4 ((CH_3)$_2$*C*(O)$_2$), 118.2 (CH=*C*H_2), 133.7 (OCH_2*C*H=CH_2).

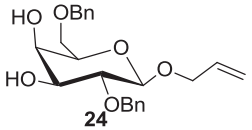
4.28. Allyl 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-β-D-galactopyranoside 23[49]



Prepared using general procedure A using allyl 3,4-*O*-isopropylidene-β-D-galactopyranoside **22** (1.0 g, 3.85 mmol, 1 equiv), sodium hydride (0.28 g, 11.55 mmol, 3 equiv) and benzyl bromide (1.37 mL, 11.55 mmol, 3 equiv). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1:9) gave the desired product **23** as a colourless oil (1.2 g, 71%).

$[\alpha]_D^{20}$ 16.7 (*c* 1.1, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 2931, 2868, 1952, 1869, 1811, 1647, 737, 699, 607; δ_H (400 MHz, $CDCl_3$) 1.32 (3H, s, CH_3), 1.35 (3H, s, CH_3), 3.42 (1H, dd, $J_{2,3}$=5.1 Hz, $J_{2,1}$=6.6 Hz, H-2), 3.75–3.82 (2H, m, H-6a, H-6b), 3.89 (1H, dd, $J_{5,4}$=1.7 Hz, $J_{5,6a}$=5.3 Hz, H-5), 4.09–4.17 (3H, m, H-3, H-4, OC*H*HCH_X=CH_2), 4.36 (1H, d, $J_{1,2}$=8.1 Hz, H-1), 4.42 (1H, ddd, $J_{vicinal}$=5.08 Hz, $J_{geminal}$=11.4 Hz, $J_{allylic}$=1.5 Hz, OC*H*HCH_X=CH_2), 4.55 and 4.80 (2H, 2d, *J*=11.8 Hz, PhCH_2), 4.64 and 4.86 (2H, 2d, *J*=11.6 Hz, PhCH_2), 5.20 (1H, ddd, $J_{allylic}$=1.5 Hz, $J_{A,X}$=10.4 Hz, $J_{A,B}$=1.6 Hz, O$CH_2$$CH_X$=C*H*$_AH_B$), 5.34 (1H, ddd, $J_{allylic}$=1.7 Hz, $J_{A,X}$=17.2 Hz, $J_{A,B}$=1.6 Hz, O$CH_2$$CH_X$=$CH_A$*H*$_B$), 5.90–6.01 (1H, m, O$CH_2$C*H*$_X$=$CH_2$), 7.20–7.42 (10H, m, 10×*CH* arom.); δ_C (100 MHz $CDCl_3$) 26.4 (CH_3), 27.8 (CH_3), 69.5 (C-6), 69.9 (O$CH_2$$CH_X$=$CH_2$), 72.7 (C-5), 73.56 ($CH_2$), 73.62 ($CH_2$), 73.8 (*C*H), 79.0 (*C*H), 79.5 (C-2), 101.9 (C-1), 109.9 ((CH_3)$_2$*C*(O)$_2$), 117.2 (O$CH_2$$CH_X$=*C*H$_AH_B$), 127.5, 127.6, 127.7, 128.2, 128.3, 128.4, 133.9 (OCH_2*C*H=CH_2), 138.2, 138.3; HRFABMS: *m*/*z* calcd for [$C_{26}H_{32}O_6$+Na]$^+$ 463.2097; found for [M+Na]$^+$: 463.2085.

4.29. Allyl 2,6-di-*O*-benzyl-β-D-galactopyranoside 24[49]

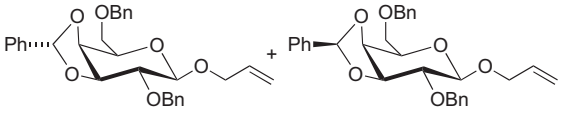


24

Allyl 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-β-D-galactopyranoside **23** (4.3 g, 9.78 mmol) was treated with 1:7 1 M aqueous hydrochloric acid/methanol (80 mL) and the reaction mixture was allowed to stir until it had reached completion by TLC (ca. 32 h). The resulting solution was quenched with 2 M aqueous sodium hydrogen carbonate (5.5 mL) and the methanol removed under reduced pressure. The resulting aqueous suspension was extracted with dichloromethane (3×40 mL) and the combined organic extracts dried ($MgSO_4$) and filtered. The solvents were removed under reduced pressure to give the desired product **24** (3.16 g, 81%) as a colourless solid.

$[\alpha]_D^{21}$ 7.4 (*c* 1.0, $CHCl_3$), lit. $[\alpha]_D$ 7 (*c* 1.0, $CHCl_3$); ν_{max} (film, neat)/cm^{-1} 3317, 2911, 2866, 1949, 1865, 1809, 1645, 733, 699; δ_H (400 MHz, $CDCl_3$) 2×–O*H* exchange, 3.50–3.60 (3H, m, H-2, H-3, H-4), 3.68–3.91 (2H, m, H-6a, H-6b), 3.86 (1H, m, H-5), 4.13 (1H, dd, $J_{vicinal}$=6.0 Hz, $J_{geminal}$=12.9 Hz, OC*H*HCH_X=CH_2), 4.40 (1H, d, $J_{1,2}$=7.12 Hz, H-1), 4.44 (1H, dd partially obscured, $J_{vicinal}$=5.1 Hz, OCH*H*CH_X=CH_2), 4.57 (2H, m≈s, PhCH_2), 4.67 and 4.96 (2H, 2d, *J*=11.4 Hz, PhCH_2), 5.19 (1H, dd, $J_{A,B}$=1.1 Hz, $J_{A,X}$=10.4 Hz, O$CH_2$$CH_X$=C*H*$_AH_B$), 5.33 (1H, dd, $J_{A,B}$=1.5 Hz, $J_{A,X}$=17.2 Hz, –O$CH_2$$CH_X$=$CH_A$*H*$_B$), 5.88–5.99 (1H, m, O$CH_2$C*H*$_X$=$CH_2$), 7.22–7.36 (10H, m, 10×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 68.9 (OC*H*HCH_X=, C-5), 69.3 (C-6), 73.1 (*C*H), 73.3 (*C*H), 73.6 (CH_2), 74.6 (CH_2), 79.1 (*C*H), 102.6 (C-1), 117.2 (CH_X=CH_2), 127.7, 127.8, 127.9, 128.1, 128.4, 128.5, 134.0 (CH_X=CH_2), 137.9, 138.4; HRFABMS: *m*/*z* calcd for [$C_{23}H_{28}O_6$–H]$^+$ 399.1808; found for [M–H]$^+$: 399.1816.

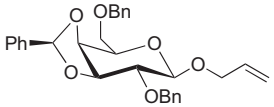
4.30. Allyl 2,6-di-*O*-benzyl-3,4-*O*-benzylidene-β-D-galactopyranosides 25a and 25b



25b: 79% **25a:** 12%

Benzaldehyde dimethyl acetal (4.25 mL, 36.2 mmol, 19 equiv), allyl 2,6-di-*O*-benzyl-β-D-galactopyranoside **24** (735 mg, 1.91 mmol, 1 equiv) and *para*-toluenesulfonic acid (138 mg, 0.73 mmol, 0.4 equiv) were dissolved in anhydrous acetonitrile (10 mL). The reaction mixture was allowed to stir at room temperature for 48 h. Triethylamine (101 μl, 0.73 mmol, 0.4 equiv) was added and the resulting mixture stirred for a further 30 min at room temperature. The solvent was removed under reduced pressure and the oily residue was purified using silica gel column chromatography (eluent gradient: ethyl acetate/light petroleum 1:99 to 15:85) to give the desired product as a pair of epimers [first eluting **25a** as a colourless solid (0.41 g, 12%) and second eluting **25b** as a colourless solid (2.81 g, 79%)].

4.30.1. *First eluting epimer **25a**.*

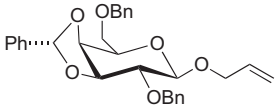


25a: 12%

Mp 108–110 °C (decomp.); $[\alpha]_D^{20}$ +61 (*c* 0.97, $CHCl_3$); ν_{max} (film, CH_2Cl_2)/cm^{-1} 3089, 3028, 1964, 1886, 1818, 1646, 735, 697; δ_H

(400 MHz, $CDCl_3$) 3.50 (1H, dd, $J_{2,1}$=8.0 Hz, $J_{2,3}$=6.2 Hz, H-2), 3.79–3.91 (2H, m, H-6a, H-6b), 3.96–4.02 (1H, m, H-5), 4.11–4.10 (1H, m, OC*H*HCH$_X$=CH$_2$), 4.22 (1H, dd, $J_{4,3}$=6.2 Hz, $J_{4,5}$=2.2 Hz, H-4), 4.32 (1H, dd≈t, $J_{3,2}$=$J_{3,4}$=6.2 Hz, H-3), 4.38–4.44 (1H, m, OCH*H*CH$_X$=CH$_2$), 4.45 (1H, d, $J_{1,2}$=8.0 Hz, H-1), 4.51 and 4.63 (2H, 2d, J=11.9 Hz, PhC*H*$_2$), 4.72 and 4.79 (2H, 2d, J=11.6 Hz, PhC*H*$_2$), 5.20 (1H, ddd, $J_{allylic}$=1.3 Hz, $J_{A,B}$=1.7 Hz, $J_{A,X}$=10.4 Hz, CH$_X$=C*H*$_A$H$_B$), 5.34 (1H, ddd, $J_{allylic}$=1.7 Hz, $J_{A,B}$=1.7 Hz, $J_{B,X}$=18.9 Hz, CH$_X$=CH$_A$*H*$_B$), 5.88 (1H, s, PhC*H*(O)$_2$), 5.88–5.96 (1H, m, OCH$_2$C*H*$_X$=CH$_2$), 7.26–7.34 (15H, m, 15×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 69.3 (C-6), 70.0 (O*C*H$_2$CH$_X$=CH$_2$), 72.0 (C-5), 73.5 (*C*H$_2$), 73.6 (*C*H$_2$), 76.2 (C-4), 78.7 (C-3), 80.2 (C-2), 101.9 (C-1), 104.6 (Ph*C*H(O)$_2$), 117.3 (OCH$_2$*C*H$_X$=CH$_2$), 126.3, 127.61, 127.64, 128.1, 128.3, 128.4, 129.1, 134.0 (OCH$_2$*C*H$_X$=CH$_2$), 137.2, 138.1, 138.2; *m*/*z* calcd for $[C_{30}H_{32}O_6]^+$ 488.2199; found for $[M]^+$: 488.2198.

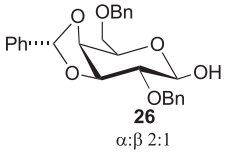
4.30.2. Second eluting epimer ***25b****.*



25b: 79%

Mp 103 °C (decomp.); $[\alpha]_D^{20}$ +25 (*c* 1.03, $CHCl_3$); ν_{max} (film, CH_2Cl_2)/cm^{-1} 3064, 2905, 1963, 1883, 1819, 1648; δ_H (400 MHz, $CDCl_3$) 3.57 (1H, dd≈t, $J_{3,2}$=$J_{3,4}$=7.0 Hz, H-3), 3.78–3.92 (3H, m, H-6a, H-6b, H-5), 4.13–4.23 (2H, m, H-2, OC*H*HCH$_X$=CH$_2$), 4.99–4.53 (3H, m, H-1, H-4, OCH*H*CH$_X$=CH$_2$), 4.53 and 4.61 (2H, 2d, J=11.4 Hz, PhC*H*$_2$), 4.84 and 4.92 (2H, 2d, J=11.6 Hz, PhC*H*$_2$), 5.27 (1H, dd, $J_{A,B}$=1.6 Hz, $J_{A,X}$=11.3 Hz, CH$_X$=C*H*$_A$H$_B$), 5.30 (1H, dd, $J_{B,A}$=1.6 Hz, $J_{B,X}$=16.0 Hz, CH$_X$=CH$_A$*H*$_B$), 5.91–5.99 (2H, m, C*H*$_X$=CH$_A$H$_B$, PhC*H*(O)$_2$), 7.19–7.45 (15H, m, 15×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 69.7 (C-6), 70.1 (O*C*H$_2$CH$_X$=CH$_2$), 72.6 (C-5), 73.6 (*C*H$_2$), 73.8 (*C*H$_2$), 74.0 (C-3), 80.17 (C-4), 80.19 (C-2), 101.8 (C-1), 103.4 (Ph*C*H(O)$_2$), 117.3 (CH$_X$=*C*H$_2$), 126.8, 127.6, 127.7, 127.9, 128.0, 128.2, 128.3, 128.4, 129.7, 134.0 (*C*H$_X$=CH$_2$), 138.17, 138.20, 138.5; HRFABMS: *m*/*z* calcd for *m*/*z* calcd for $[C_{30}H_{32}O_6]^+$ 488.2199; found for $[M]^+$: found 488.2210.

4.31. 2,6-Di-*O*-benzyl–3,4-*O*-benzylidene-β-D-galactopyranose 26

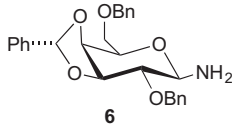


26
α:β 2:1

Allyl 2,6-di-*O*-benzyl-3,4-*O*-benzylidene-β-D-galactopyranoside **25b** (1.0 g, 2.05 mmol, 1 equiv) and 1,4-diazabicyclo[2.2.2]octane (42.8 mg, 0.40 mmol, 20 mol %) were dissolved in 95:5 ethanol/water and the reaction mixture was degassed. Wilkinson's catalyst (90 mg, 0.098 mmol, 5 mol %) was then added. The solution was heated for 21 h at 80 °C after which time it was allowed to cool to room temperature. The solvents were removed under reduced pressure and the resulting residue dissolved in dichloromethane (5 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford the crude enol ether. The crude enol ether was dissolved in tetrahydrofuran (30 mL), water (8 mL) and pyridine (0.8 mL) and iodine (2.23 g, 12.7 mmol, 6.2 equiv) was added. The solution was stirred for 10 min at ambient temperature. After this period, the reaction mixture was cooled to 0 °C and treated with 10% aqueous sodium thiosulfite (5 mL). After 15 min at 0 °C the solution was extracted with ethyl acetate (3×35 mL). The combined aqueous extracts were washed with 10% aqueous sodium thiosulfite (2×5 mL) and water (5 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was purified using silica gel column chromatography (eluent: ethyl acetate/light petroleum 2:3) to give the desired product **26** (587 mg, 64%) as a colourless solid and a mixture of anomers (α/β 2:1 by ^{1}H NMR).

Mp 137.6 °C (decomp.); $[\alpha]_D^{21}$ 0.8 (*c* 1.5, $CHCl_3$). Found C 72.36, H 6.21. $C_{27}H_{28}O_6$ requires C 72.30, H 6.29; ν_{max} (film, $CHCl_3$)/cm^{-1} 3386, 3087, 3030, 1954, 1813, 736, 698; δ_H (400 MHz, $CDCl_3$) −O*H*β exchange, 3.51 (1H, dd≈t, $J_{2,1}$=$J_{2,3}$=7.1 Hz, H-2β), 3.65–3.87 (3H, m, H-6aα, H-6bα, H-6aβ), 3.67 (1H, dd, $J_{2,1}$=3.8 Hz, $J_{2,3}$=7.1 Hz, H-2α), 3.76 (1H, t, J=7.6 Hz, H-6bβ), 3.86–3.92 (1H, m, H-5β), 4.09 (1H, dd, $J_{4,5}$=1.8 Hz, $J_{4,3}$=5.6 Hz, H-4β), 4.12 (1H, dd, $J_{4,5}$=2.2 Hz, $J_{4,3}$=5.6 Hz, H-4α), 4.27 (1H, br s, −O*H*α), 4.39–4.45 (2H, m, H-3β, H-5α), 4.47 and 4.61 (2H, 2d, J=12.2 Hz, PhC*H*$_2$β), 4.48 and 4.60 (2H, 2d, J=12.2 Hz, PhC*H*$_2$α), 4.68 (1H, dd, $J_{3,2}$=7.1 Hz, $J_{3,4}$=5.6 Hz, H-3α), 4.70 (1H, d, partially overlapped, H-1β), 4.76 and 4.81 (2H, 2d, J=12.2 Hz, PhC*H*$_2$α), 4.86 and 4.88 (each 2H, d, J=11.7 Hz, PhC*H*$_2$β), 5.29 (1H, d, $J_{1,2}$=3.8 Hz, H-1α), 5.94 (1H, s, PhC*H*(O)$_2$β), 5.94 (1H, s, PhC*H*(O)$_2$α), 7.14–7.43 (30H, m, 15×C*H*α arom., 15×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 66.8 (C-5α), 69.4 (C-6α), 69.6 (C-6β), 72.2 (C-5β), 72.6 (*C*H$_2$α), 73.2 (C-2α), 73.3 (*C*H$_2$β), 73.4 (*C*H$_2$α), 73.5 (*C*H$_2$β), 73.7 (C-4α), 74.0 (C-4β), 74.7 (C-3α), 77.6 (C-2β), 79.7 (C-3β), 90.8 (C-1α), 96.2 (C-1β), 103.1 (Ph*C*H(O)$_2$α), 103.2 (Ph*C*H(O)$_2$β), 126.1, 126.4, 127.78, 127.83, 127.9, 128.1, 128.19, 128.24, 128.38, 128.44, 128.5, 128.6, 129.2, 137.7, 137.9, 138.9; HRFABMS: *m*/*z* calcd for $[C_{27}H_{28}O_6]^+$: 448.1886; found for $[M]^+$: 448.1881.

4.32. 1-Amino-2,6-di-*O*-benzyl-3,4-benzylidene-1-deoxy-D-galactopyranose 6

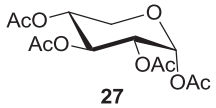


6
α:β 0.6:1

Prepared using general procedure C using 2,6-di-*O*-benzyl-3,4-benzylidene-D-galactopyranose **26** (3 g, 6.71 mmol). Silica gel column chromatography (eluent: trriethylamine/ethyl acetate/light petroleum 1:59:40) gave the desired product **6** as a colourless solid (1.89 g, 63%) as a mixture of anomers (α/β 0.6:1 by ^{1}H NMR).

Mp 96.2 °C (decomp.); $[\alpha]_D^{22}$ 6.5 (*c* 1.0, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 3368, 3031, 1955, 1880, 1812, 741, 697; δ_H (400 MHz, $CDCl_3$) −N*H*$_2$α exchanging, 2.02 (2H, br s, N*H*$_2$β), 3.35 (1H, dd, $J_{2,3}$=6.0 Hz, $J_{2,1}$=7.3 Hz, H-2β), 3.52–3.63 (2H, m, H-6aα, H-6bα), 3.52–3.38 (2H, m, H-6aβ, H-6bβ), 3.80 (1H, dd, $J_{2,1}$=3.8 Hz, $J_{2,3}$=6.2 Hz H-2α), 4.05 (1H, dd, $J_{5,4}$=2.16 Hz, $J_{5,6a}$=6.0 Hz, H-5β), 4.22 (1H, d partially overlapped, H-1β), 4.23 (1H, dd partially overlapped, $J_{4,3}$=4.5 Hz, H-4β), 4.28 (1H, dd, $J_{5,4}$=1.8 Hz, $J_{5,6b}$=7.4 Hz, H-5α), 4.38 (1H, dd, $J_{3,2}$=6.0 Hz, $J_{3,4}$=4.5 Hz H-3β), 4.41–4.44 (1H, m, H-4α), 4.45 (1H, dd partially overlapped, $J_{3,4}$=4.0 Hz, H-3α), 4.51 (1H, d, J=12.2 Hz, PhC*H*Hβ), 4.52 (1H, d, J=12.1 Hz, PhC*H*Hβ), 4.63 (1H, d, J=12.1 Hz, PhCH*H*α), 4.64 (1H, d, J=11.1 Hz, PhCH*H*β), 4.69 (4H, m, PhC*H*$_2$α, PhC*H*$_2$β), 4.93 (1H, d, $J_{1,2\alpha}$=3.6 Hz, H-1α), 5.77 (1H, s, PhC*H*(O)$_2$α), 5.86 (1H, s, PhC*H*(O)$_2$β), 7.10–7.42 (26H, m, 13×C*H*α arom., 13×C*H*β arom.), 7.42–7.56 (4H, m, 2×C*H*α arom., 2×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 68.0 (C-5α), 69.6 (C-6β), 70.0 (C-6α), 72.3 (C-5β), 72.8 (*C*H$_2$β), 73.56 (*C*H$_2$α), 73.59 (*C*H$_2$α), 73.66 (C-3α), 73.67 (*C*H$_2$β), 74.4 (C-4α), 76.0 (C-2α), 76.2 (C-4β), 78.3 (C-1α), 78.7 (C-3β), 80.1 (C-2β), 84.8 (C-1β), 104.3 (Ph*C*H(O)$_2$α), 104.5 (Ph*C*H(O)$_2$β), 127.0, 127.1, 127.68, 127.76, 127.79, 127.87, 127.89, 127.93, 128.0, 128.3, 128.39, 128.41, 128.42, 128.44, 128.47, 128.55, 129.4, 129.7, 136.9, 137.3, 137.4, 138.0, 138.1, 138.2; *m*/*z* calcd for $[C_{27}H_{29}NO_5+H]^+$: 448.2124; found for $[M+H]^+$: 448.2120.

4.33. 1,2,3,4-Tetra-*O*-acetyl-α-D-xylopyranose 27[50]

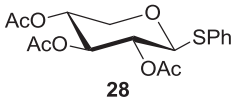


27

D-Xylose (7.0 g, 46.7 mmol, 1 equiv) and 4-(dimethylamino) pyridine (0.28 g, 2.3 mmol, 5 mol %) were dissolved in pyridine (350 mL). Acetic anhydride (35.3 mL, 374.0 mmol, 8 equiv) was added. The reaction mixture was allowed to stir overnight. Then, water (250 mL) was added, and the resulting mixture was left to stir for a further hour, after which time it was extracted with dichloromethane (3×20 mL). The combined extracts were concentrated under reduced pressure, washed with aqueous saturated sodium hydrogen carbonate, dried ($MgSO_4$) and filtered. The filtrate was concentrated under reduced pressure and purified using silica gel column chromatography (eluent: light petroleum/ethyl acetate 3:2) to afford **27** (13.9 g, 94%) as a colourless oil.

$[\alpha]_D^{20}$ 33 (*c* 1.1, $CHCl_3$), lit. $[\alpha]_D^{15}$ 25.7 (*c* 4.0, $CHCl_3$); ν_{max} (neat)/cm^{-1} 2961, 2898, 1751, 1437, 1369, 937; δ_H (400 MHz, $CDCl_3$) 2.03 (3H, s, CH_3CO), 2.06 (3H, s, CH_3CO), 2.18 (3H, s, CH_3CO), 2.19 (3H, s, CH_3CO), 3.72 (1H, dd, *J*=11.0 Hz, H-5a), 3.94 (1H, dd $J_{5b,4}$=6.0 Hz, $J_{5b,5a}$=11.0 Hz, H-5b), 4.99–5.07 (2H, m, H-2, H-4), 5.47 (1H, dd, $J_{3,2}$=$J_{3,4}$ 10.0 Hz, H-3), 6.26 (1H, d, $J_{1,2}$=3.6 Hz, H-1); δ_C (100 MHz, $CDCl_3$) 20.5 (*C*H_3CO), 20.7 (*C*H_3CO); 20.8 (*C*H_3CO), 20.9 (*C*H_3CO), 60.6 (C-5), 68.7 (C-3), 69.3 (*C*H), 69.5 (*C*H), 92.0 (C-1), 169.0 (CH$_3$*C*O), 169.7 (CH$_3$*C*O), 169.8 (CH$_3$*C*O), 170.1 (CH$_3$*C*O); HRFABMS: *m*/*z* calcd for $[C_{13}H_{18}O_9+Na]^+$: 341.0848; found for $[M+Na]^+$: 341.0851.

4.34. Phenyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside 28[51]

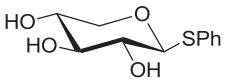


28

1,2,3,4-Tetra-*O*-acetyl-α-D-xylopyranose **27** (8.5 g, 26.7 mmol, 1 equiv) was dissolved in anhydrous dichloromethane (50 mL) under a nitrogen atmosphere. Thiophenol (4.11 mL, 41 mmol, 1.5 equiv) was then added dropwise. The resulting solution was cooled to 0 °C and ethereal boron trifluoride (8.5 mL, 66.8 mmol, 2.5 equiv) was added dropwise over 50 min. The reaction mixture was allowed to warm to room temperature and left to stir for 24 h after which time it was treated with aqueous saturated aqueous sodium hydrogen carbonate (210 mL) and extracted with dichloromethane (3×50 mL). The combined extracts were washed with water (60 mL) and dried ($MgSO_4$). After filtration, the filtrate was concentrated in vacuo and purified using silica gel column chromatography (eluent: light petroleum/ethyl acetate 7:3) to afford the desired product **28** (8.6 g, 87%) as a colourless oil.

$[\alpha]_D^{24}$ −51.6 (*c* 1.0, $CHCl_3$), lit. $[\alpha]_D^{23}$ −54.9 (*c* 1.0, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3057, 2950, 2867, 1752, 1583, 1439, 876, 822; δ_H (400 MHz, $CDCl_3$) 2.05 (6H, s, 2×CH_3CO), 2.10 (3H, s, CH_3CO), 3.43 (1H, dd, $J_{5a,4}$,=8.8 Hz, $J_{5a,5b}$=12.0 Hz, H-5a), 4.28 (1H, dd, $J_{5b,4}$=4.8 Hz, $J_{5b,5a}$=12.0 Hz, H-5b), 4.81 (1H, d, $J_{1,2}$=8.4 Hz, H-1), 4.91–4.97 (2H, m, H-2, H-4), 5.19 (1H, dd, $J_{3,2}$=$J_{3,4}$=8.0 Hz, H-3), 7.27–7.33 (3H, m, 3×C*H* arom.), 7.46–7.50 (2H, m, 2×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 20.72 (*C*H$_3$CO), 20.73 (*C*H$_3$CO), 20.8 (*C*H$_3$CO), 65.2 (C-5), 68.4 (*C*H), 69.8 (*C*H), 72.0 (C-3), 86.2 (C-1), 128.2, 129.1, 133.9, 169.3 (CH$_3$*C*O), 169.8 (CH$_3$*C*O), 169.9 (CH$_3$*C*O); HRFABMS: *m*/*z* calcd for $[C_{17}H_{20}O_7S+H]^+$: 369.1008; found for $[M+H]^+$: 369.1010.

4.35. Phenyl 1-thio-β-D-xylopyranoside 29[52]

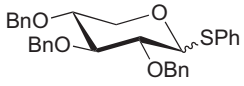


29

A 3 M solution of sodium methoxide was prepared by dissolving sodium methoxide (16.2 g, 300 mmol) in dried freshly distilled methanol (100 mL). Phenyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-xylopyranoside **28** (8.0 g, 21.7 mmol) was dissolved in dry methanol (100 mL) followed by the addition of 10 mL of 3 M sodium methoxide solution. The reaction mixture was stirred at room temperature under nitrogen until the reaction had reached completion by TLC (ca. 1 h). After this period Amberlite IR 120 H^+ cation exchange resin was added until neutralisation was effected. The resin was then removed by filtration and the filtrate concentrated under reduced pressure. The resulting residue was purified by triturating and washing with dichloromethane to give the desired compound **29** (4.52 g, 86%) as a colourless solid.

Mp 136–138 °C (lit. mp 138 °C); $[\alpha]_D^{24}$ −70.2 (*c* 1.0, methanol), lit. $[\alpha]_D^{21}$ −78.9 (*c* 3.0, methanol); ν_{max} (KBr)/cm^{-1} 3397, 2862, 2002, 1941, 1860, 1784, 959, 837; δ_H (400 MHz, $(CD_3)_2SO$) 3.11 (1H, dd, $J_{2,1}$=$J_{2,3}$=9.4 Hz, H-2), 3.02–3.24 (2H, m, H-4, H-5b), 3.30–3.50 (1H, m, H-5a), 3.82 (1H, dd, $J_{3,2}$=9.4 Hz, $J_{3,4}$=5.0 Hz, H-3), 4.65 (1H, d, $J_{1,2}$=9.4 Hz, H-1), 5.06 (1H, br s, −O*H*), 5.15 (1H, br s, −O*H*), 5.72 (1H, br s, −O*H*), 7.25–7.45 (5H, m, 5×C*H* arom.); δ_C (100 MHz, $(CD_3)_2SO$) 68.9 (C-5), 69.2 (C-3), 72.2 (C-2), 79.1 (C-4), 87.6 (C-1), 126.5, 128.8, 130.1, 134.2; HRFABMS: *m*/*z* calcd for $[C_{11}H_{14}O_4S]^+$: 242.0613; found for $[M]^+$: 242.0617.

4.36. Phenyl 2,3,4,-tri-benzyl-1-thio-D-xylopyranoside 30[52]

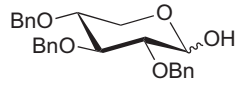


30
α:β 1.2

Prepared using general procedure A using phenyl 1-thio-β-D-xylopyranoside **29** (4.77 g, 18.2 mmol, 1 equiv), sodium hydride (1.97 g, 81.9 mmol, 4.5 equiv) and benzyl bromide (9.74 mL, 81.9 mmol, 4.5 equiv). Silica gel column chromatography (eluent: ethyl acetate/light petroleum 1:9) gave the desired product **30** as a yellow oil (6.2 g, 67%) and a mixture of anomers (α/β 1:2 by ^1H NMR).

$[\alpha]_D^{21}$ 49.8 (*c* 1.4, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3028, 2866, 1950, 1816, 1809, 1752, 1453, 1074, 738, 697; δ_H (400 MHz, $CDCl_3$) 3.18–3.30 (1H, m, H-5aβ), 3.41–3.50 (1H, m, H-4β), 3.53–3.73 (4H, m, H-2β, H-3α, H-3β, H-5aα), 3.77–3.89 (2H, m, H-2β, H-4β), 4.00–4.09 (2H, m, H-5bα, H-5bβ), 4.57–4.93 (13H, m, 3×PhCH_2α, 3×PhCH_2β, H-1β), 5.54 (1H, br s, H-1α), 7.14–7.62 (40H, m, 20×C*H*α arom., 20×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 61.5 (C-5α), 67.9 (C-5β), 73.1 (*C*H$_2$α), 73.7 (*C*H$_2$β), 74.0 (*C*H$_2$α), 75.9 (*C*H$_2$β), 76.1 (*C*H$_2$β), 76.2 (*C*H$_2$α), 78.1 (C-3α), 78.2 (C-3β), 80.0 (*C*Hα), 80.9 (C-4β), 82.1 (*C*Hα), 85.8 (C-2β), 87.8 (C-1α), 88.9 (C-1β), 127.6, 128.0, 128.1, 128.2, 128.28, 128.31, 128.4, 128.5, 128.6, 128.7, 128.8, 128.9, 129.0, 129.4, 132.0, 132.4, 138.2, 138.5, 138.7, 138.9, 139.2; HRFABMS: *m*/*z* calcd for $[C_{32}H_{32}O_4S-H]^+$: 511.1943; found for $[M-H]^+$: 511.1936.

4.37. 3,4,5-Tri-*O*-benzyl-D-xylose 31[53]

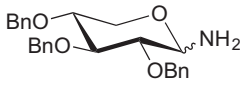


31
α:β 1:2

N-Bromosuccinimide (3.34 g, 18.7 mmol, 1.6 equiv) was added to a solution of phenyl 2,3,4,-tri-*O*-benzyl-1-thio-D-xylopyranoside **30** (6.0 g, 11.7 mmol, 1 equiv) in acetone (45 mL) at −15 °C in the dark. After 45 min, the reaction was quenched by the addition of a solution of saturated aqueous sodium hydrogen carbonate. The resulting mixture was extracted with ethyl acetate (3×15 mL). The combined organic extracts were washed with water (50 mL), dried ($MgSO_4$) and concentrated in vacuo. The residue was purified using silica gel column chromatography (eluent: light petroleum/ethyl acetate 3:2) to furnish **31** (3.5 g, 72%) as a colourless solid and a mixture of anomers (α/β 1:2 by ^{1}H NMR).

$[\alpha]_D^{24}$ 10 (*c* 1.0, $CHCl_3$); lit. $[\alpha]_D^{15}$ 12 (*c* 1.49, $CHCl_3$); ν_{max}/cm^{-1} (film, CH_2Cl_2) 3028, 2866, 1950, 1816, 1809, 1752, 1453, 1074, 738, 697; δ_H (400 MHz, $CDCl_3$) −O*H*α and −O*H*β exchanging, 3.18–3.50 (2H, m, H-5aβ, H-2β), 3.47 (1H, dd, $J_{2,1}$=3.6 Hz, $J_{2,3}$=9.2 Hz, H-2α), 3.53–3.73 (4H, m, H-3β, H-4α, H-4α, H-5aα), 3.77–3.89 (3H, m, H-3α, H-5bα, H-5bβ), 4.55–4.63 (7H, m, 3×PhCH_2, H-1β), 4.80–4.91 (6H, m, 3×PhCH_2), 5.09 (1H, s, H-1α), 7.21–7.41 (30H, m, 15×C*H*α arom., 15×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 60.7 (C-5α), 64.1 (C-5β), 73.6 (CH_2β), 73.7 (CH_2α), 73.8 (CH_2α), 75.2 (CH_2β), 75.9 (CH_2β), 76.0 (CH_2α), 77.76 (C-3β), 77.79 (C-4α), 79.8 (C-2α), 80.9 (C-3α), 82.8 (C-2β), 83.6 (C-4β), 91.8 (C-1α), 98.2 (C-1β), 127.7, 127.8, 127.86, 127.87, 127.93, 128.02, 128.05, 128.09, 128.13, 128.44, 128.46, 128.49, 128.52, 128.55, 137.8, 138.2, 138.57, 138.64, 138.9; HRFABMS: *m*/*z* calcd for $[C_{26}H_{28}O_5+Na]^+$: 443.1834; found for $[M+Na]^+$: 443.1843.

4.38. 1-Amino-3,4,5-tri-*O*-benzyl-D-xylose 7

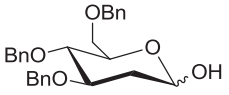


7
α:β 1:2

Prepared using general procedure C using 3,4,5-tri-*O*-benzyl-D-xylose **31** (6.33 g, 14.3 mmol). Silica gel column chromatography (eluent: triethylamine/ethyl acetate/light petroleum 1:59:40) gave the desired product **7** as a colourless solid (1.86 g, 62%) as a mixture of anomers (α/β 1:2 by ^{1}H NMR).

Mp 91.4–93.1 °C (decomp.); $[\alpha]_D^{25}$ 118 (*c* 1.0, $CHCl_3$). Found C 74.20, H 6.74, N 2.91. $C_{26}H_{29}O_4N$ requires C 74.44, H 6.97, N 3.34; ν_{max} (film, $CHCl_3$)/cm^{-1} 3390, 3327, 2894, 1951, 1875, 1810, 1077; δ_H (400 MHz, $CDCl_3$) with −NH_2α and −NH_2β exchanging, 3.15–3.34 (2H, m, H-2β, H-5aβ), 3.47 (1H, dd, $J_{2,1}$=3.6 Hz, $J_{2,3}$=9.2 Hz, H-2α), 3.50–3.62 (2H, m H-4α, H-4β), 3.65 (1H, dd, $J_{5a,4}$=$J_{5a,5b}$=9.2 Hz, H-5aα), 3.79 (1H, dd, $J_{5b,4}$=5.8 Hz, $J_{5b,5a}$=9.2 Hz, H-5bα), 3.85 (1H, dd, *J*=9.2 Hz, H-3α), 3.92 (1H, dd, $J_{5b,4}$=5.6 Hz, $J_{5b,5a}$=13.3 Hz, H-5bβ), 4.59–4.64 (8H, m, 7×PhC*H*H, H-1β), 4.80–4.91 (5H, m, 5×PhC*H*H), 5.09 (1H, d, $J_{1,2}$=3.6 Hz, H-1α), 7.21–7.41 (30H, m, 15×C*H*α, 15×C*H*β); δ_C (100 MHz, $CDCl_3$) 64.13 (C-5β), 64.14 (C-5α), 73.6 (CH_2α), 73.7 (CH_2β), 73.8 (CH_2α), 75.2 (CH_2β), 75.9 (CH_2β), 76.0 (CH_2α), 77.9 (C-4α), 78.0 (C-3β), 79.8 (C-2α), 80.9 (C-3α), 82.8 (C-2β), 83.6 (C-4β), 91.8 (C-1α), 98.2 (C-1β), 127.6, 127.66, 127.69, 127.81, 127.85, 127.9, 128.0, 128.12, 128.15, 128.35, 128.37, 128.44, 138.1, 138.3, 138.4, 138.6; HRFABMS: *m*/*z* calcd for $[C_{26}H_{29}O_4N+H]^+$: 420.2177; found for $[M+H]^+$: 420.2177.

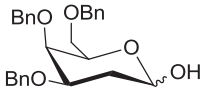
4.39. 3,4,6-Tri-*O*-benzyl-2-deoxy-D-*arabino*-hexopyranose 33a[54]



3,4,6-Tri-*O*-benzyl-D-galactal **32a** (1.1 g, 2.64 mmol) was dissolved in 90:10:1 tetrahydrofuran/water/8 M hydrochloric acid (20 mL) and allowed to stir at room temperature until all the starting material had been consumed. The reaction mixture was neutralised with sodium hydroxide pellets, and the tetrahydrofuran removed under reduced pressure. The resulting aqueous slurry was extracted with dichloromethane (3×50 mL) and the combined organic extracts were dried ($MgSO_4$) and filtered. Evaporation of dichloromethane from the filtrate yielded the desired product **33a** (1.24 g, 83%) as a colourless solid and a mixture of anomers (α/β 4:1 by ^{1}H NMR)

Mp 100–103 °C (lit. mp 103–104 °C); $[\alpha]_D^{21}$ 47.6 (*c* 1.0, $CHCl_3$) [lit. $[\alpha]_D$ 48.2 (no conditions stated)]; ν_{max} (film, CH_2Cl_2)/cm^{-1} 3406, 2868, 1951, 1876, 1809, 1496, 1364, 1102, 736, 697; δ_H (400 MHz, $CDCl_3$) O*H*α and O*H*β exchange, 1.55 (1H, td, *J*=9.8, 11.8, 9.8 Hz, H-2aβ), 1.66 (1H, td, *J*=3.6, 11.6 Hz, 13.0 Hz, H-2aα), 2.21–2.33 (2H, m, H-2bα, H-2bβ), 3.40–3.78 (8H, m, H-3β, H-4α, H-4β, H-5β, H-6aα, H-6aβ, H-6bα, H-6β), 4.0–4.11 (2H, m, H-3α, H-5α), 4.42–4.71 (11H, m, H-1β, 5×PhC*H*Hα, 5×PhC*H*Hβ), 4.87 (1H, d, *J*=10.8 Hz, PhC*H*Hβ), 4.89 (1H, d, *J*=11.0 Hz, PhC*H*Hα), 5.36 (1H, d, $J_{1,2}$=3.6 Hz, H-1α), 7.04–7.45 (30H, m, 15×C*H*α arom., 15×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 35.5 (C-2α), 37.6 (C-2β), 55.80 (C-6β), 55.84 (C-6α), 69.3 (C-5α), 70.6 (CH_2β), 71.37 (CH_2β), 71.39 (CH_2α), 73.4 (CH_2α), 74.7 (*C*Hβ), 74.86 (CH_2α), 74.87 (CH_2β), 76.7 (C-3α), 77.0 (*C*Hβ), 77.1 (C-4α), 79.2 (*C*Hβ), 92.0 (C-1α), 94.8 (C-1β), 127.55, 127.58, 127.65, 127.67, 127.9, 128.0, 128.30, 128.35, 128.37, 128.42, 137.9, 138.3, 138.6, 138.4, 140.1; HRFABMS: *m*/*z* calcd for $[C_{27}H_{30}O_5-H]^+$: 433.2015; found $[M-H]^+$: 433.2017.

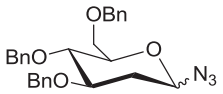
4.40. 3,4,6-Tri-*O*-benzyl-2-deoxy-D-*lyxo*-hexopyranose 33b[54]



3,4,6-Tri-*O*-benzyl-D-glucal **32b** (1.5 g, 3.61 mmol) was dissolved in 90:10:1 tetrahydrofuran/water/8 M hydrochloric acid (30 mL) and allowed to stir at room temperature until all the starting material had been consumed. The reaction mixture was neutralised with sodium hydroxide pellets, and the tetrahydrofuran removed under reduced pressure. The resulting aqueous slurry was extracted with dichloromethane (3×50 mL) and the combined organic extracts were dried ($MgSO_4$) and filtered. Evaporation of dichloromethane from the filtrate yielded the desired product **33b** (1.41 g, 90%) as a colourless solid and a mixture of anomers (α/β 4:1 by ^{1}H NMR).

Mp 76 °C (lit. mp 71–74 °C); $[\alpha]_D^{20}$ 18.6 (*c* 1.0, $CHCl_3$) [lit. $[\alpha]_D$ 18.4 (no conditions stated)]; ν_{max} (film, CH_2Cl_2)/cm^{-1} 3410, 3086, 3061, 1953, 1877, 1810, 737, 697; δ_H (400 MHz, $CDCl_3$) 1.95–2.03 (1H, m, H-2aβ), 2.05–2.12 (1H, m, H-2aα), 2.17–2.19 (1H, m, H-2bβ), 2.73–2.80 (1H, m, H-2bα), 3.32 (2H, br s, O*H*α, O*H*β), 3.43–3.59 (5H, m, H-6aα, H-6bα, H-6aβ, H-6bβ, C*H*β), 3.67–3.74 (3H, m, 2×C*H*α, H-5β), 3.97–4.01 (1H, m, H-3β), 4.12 (1H, d, *J*=3.4 Hz, H-1α), 4.41 and 4.91 (2H, 2d, *J*=11.2 Hz, PhCH_2β), 4.58 and 4.86 (2H, 2d, PhCH_2β), 4.58 and 4.86 (2H, 2d, *J*=12.6 Hz, PhCH_2β), 4.76–4.81 (9H, m, 3×PhCH_2α, PhCH_2β, C*H*α), 5.43 (1H, br s, H-1β), 7.22–7.41 (30H, m, 15×C*H*α arom., 15×CHβ arom.); δ_C (100 MHz, $CDCl_3$) 31.0 (CH_2β), 34.4 (CH_2α), 69.0 (CH_2α), 69.3 (CH_2α), 70.0 (C-5β), 70.1 (CH_2β), 70.2 (CH_2α), 70.5 (CH_2β), 71.7 (*C*Hα), 73.3 (C-4β), 73.46 (CH_2β), 73.52 (CH_2α), 74.1 (*C*Hα), 74.2 (CH_2β), 74.3 (C-3β), 77.1 (*C*Hα), 92.8 (C-1β), 94.8 (C-1α), 127.3, 127.4, 127.5, 127.7, 127.8, 127.9, 128.0, 128.1, 128.38, 128.42, 128.5, 129.1, 137.8, 137.9, 138.2, 138.5, 138.6, 138.7; HRFABMS: *m*/*z* calcd for $[C_{27}H_{30}O_5-H]^+$: 433.2015; found $[M-H]^+$: 433.2018.

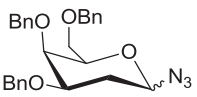
4.41. 3,4,6-Tri-*O*-Benzyl-2-deoxy-β-D-*arabino*-hexopyranosyl azide 34a



3,4,6-Tri-*O*-benzyl-2-deoxy-D-*arabino*-hexopyranose **33a** (4.6 g, 10.6 mmol, 1 equiv) and triphenylphosphine (5.6 g, 21.2 mmol, 2 equiv) were dissolved in *N*,*N*-dimethylformamide (90 mL). This was followed by the addition of sodium azide (3.5 g, 53.0 mmol, 5 equiv). The stirred mixture was then placed under a nitrogen atmosphere and cooled to 0 °C. Bromine (1.1 mL, 21.2 mmol, 2 equiv) was then added dropwise over 30 min. After this period the reaction was allowed to attain ambient overnight, after which time triethylamine (5.9 mL, 42.4 mmol, 4 equiv) was added and the mixture allowed to stir for a further 30 min. The mixture was then diluted with saturated brine (120 mL) and extracted with diethyl ether (6×50 mL). The combined organic extracts were dried ($MgSO_4$) and filtered. The diethyl ether was removed in vacuo and the residue purified by column chromatography (eluent gradient: light petroleum/ethyl acetate 94:6 to 9:1) to give the desired compound **34a** (2.1 g, 43%) as a colourless solid and a mixture of anomers (α/β≈1:4 by ^{1}H NMR).

Mp 124.4–125.2 °C (decomp.); $[\alpha]_D^{22}$ 39.4 (*c* 1.5, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 3086, 3061, 2111, 1950, 1874, 1809; δ_H (400 MHz, $CDCl_3$) 1.63 (1H, ddd, $J_{2a,1}$=9.4 Hz, $J_{2a,2b}$=12.7 Hz, $J_{2a,3}$=11.1 Hz, H-2aβ), 1.74 (1H, ddd, $J_{2a,1}$=1.8 Hz, $J_{2a,2b}$=15.1 Hz, $J_{2a,3}$=10.1 Hz, H-2aα), 2.14 (1H, ddd, $J_{2b,1}$=1.5 Hz, $J_{2b,2a}$=15.1 Hz, $J_{2b,3}$=5.2 Hz, H-2bα), 2.28 (1H, ddd, $J_{2b,1}$=2.1 Hz, $J_{2b,2a}$=12.7 Hz, $J_{2b,3}$=4.8 Hz, H-2bβ), 3.46 (1H, ddd, $J_{5,4}$=9.0 Hz, $J_{5,6a}$=$J_{5,6b}$=3.7 Hz, H-5β), 3.56 (1H, t, *J*=9.0 Hz, H-4β), 3.60–3.78 (6H, m, H-3α, H-3β, H-4α, H-6aα, H-6aβ, H-6bα), 3.80 (1H, dd, $J_{6b,5}$=3.7 Hz, $J_{6b,6a}$=10.5 Hz, H-6bβ), 3.84–3.92 (1H, m, H-5α), 4.50 (1H, d, *J*=12.2 Hz, PhC*H*Hα), 4.52 (1H, d, *J*=10.8 Hz, PhC*H*Hα), 4.54 (9H, m, H-1β, PhCH_2α, 3×PhCH_2β), 4.88 (1H, d, *J*=10.8 Hz, PhCH*H*α), 4.88 (1H, d, *J*=10.8 Hz, PhCH*H*α), 5.52 (1H, d, $J_{1,2}$=2.8 Hz, H-1α), 7.08–7.39 (30H, m, 15×C*H*α arom., 15×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 34.8 (C-2α), 36.2 (C-2β), 68.6 (C-6α), 68.8 (C-6β), 70.1 (CH_2α), 71.7 (CH_2β), 73.2 (C-5α), 73.56 (CH_2α), 73.58 (CH_2β), 75.0 (CH_2α), 75.1 (CH_2β), 76.8 (C*H*α), 77.4 (C-5β), 77.5 (C-4β), 77.7 (C*H*α), 79.2 (C-3β), 86.4 (C-1β), 87.5 (C-1α), 127.69, 127.73, 127.80, 127.85, 127.87, 127.92, 127.97, 128.05, 128.40, 128.44, 128.5, 138.15, 138.18, 138.25, 138.33, 138.39,138.40; HRFABMS: *m*/*z* calcd for $[C_{27}H_{29}N_3O_4-H]^+$: 458.2080; found for $[M-H]^+$: 458.2072.

4.42. 3,4,6-Tri-*O*-benzyl-2-deoxy-α- and β-D-lyxo-hexopyranosyl azide 34b

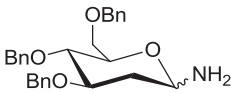


3,4,6-Tri-*O*-benzyl-2-deoxy-D-*lyxo*-hexopyranose **33b** (5.0 g, 11.1 mmol, 1 equiv) and triphenylphosphine (5.8 g, 22.2 mmol, 2 equiv) were dissolved in *N*,*N*-dimethylformamide (90 mL). This was followed by the addition of sodium azide (3.6 g, 55.5 mmol, 5 equiv). The stirred mixture was then placed under a nitrogen atmosphere and cooled to 0 °C. Bromine (1.15 mL, 22.2 mmol, 2 equiv) was then added dropwise over 30 min. After this period the reaction mixture was allowed to attain ambient overnight, after which time triethylamine (6.2 mL, 44.4 mmol, 4 equiv) was added and the mixture allowed to stir for a further 30 min. The mixture was then diluted with saturated brine (120 mL) and extracted with diethyl ether (6×50 mL). The combined organic extracts were dried ($MgSO_4$) and filtered. The diethyl ether was removed in vacuo and the residue purified by column chromatography (light petroleum/ethyl acetate 94:6–9:1) to first elute α-**34b** (371 mg, 7%) as a colourless oil followed by β-**34b** (2.49 g, 47% yield) also as a colourless oil.

*4.42.1. First eluting anomer α-**34b**.* $[\alpha]_D^{21}$ 64.4 (*c* 1.6, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3062, 3029, 2107, 1954, 1876, 1812, 737, 698; δ_H (400 MHz, $CDCl_3$) 1.85 (1H, ddd, $J_{2a,1}$=1.3 Hz, $J_{2a,3}$=4.4 Hz, $J_{2a,2b}$=12.9 Hz, H-2a), 2.26 (1H, ddd, $J_{2b,1}$=4.2 Hz, $J_{2b,2a}$=12.9 Hz, $J_{2b,3}$=12.0 Hz, H-2b), 3.57–3.64 (2H, m, H-6a, H-6b), 3.79 (1H, ddd, $J_{3,2a}$=4.4 Hz, $J_{3,2b}$=12.0 Hz, $J_{3,4}$=2.4 Hz, H-3), 3.93 (1H, br s, H-4), 4.02 (1H, t, *J*=6.6 Hz, H-5), 4.43 and 4.52 (2H, 2d, *J*=11.7 Hz, PhCH_2), 4.55–4.64 (3H, m, PhCH_2), 4.91 (1H, d, *J*=11.5 Hz, PhCH_2), 5.55 (1H, d, $J_{1,2}$=3.6 Hz, H-1), 7.20–7.45 (15H, m, 15×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 30.4 (C-2), 69.1 (CH_2), 70.5 (CH_2), 72.2 (C-5), 72.7 (C-4), 73.5 (CH_2), 74.1 (C-3), 74.4 (CH_2), 88.0 (C-1), 127.3, 127.6, 127.7, 127.8, 127.9, 128.2, 128.3, 128.4, 128.5, 137.9, 138.2, 138.6; HRFABMS: *m*/*z* calcd for $[C_{27}H_{29}N_3O_4-H]^+$: 458.2079; found for $[M-H]^+$: 458.2088.

*4.42.2. Second eluting anomer β-**34b**.* $[\alpha]_D^{21}$ 15.2 (*c* 1.5, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3086, 3062, 2107, 1953, 1876, 1812, 736, 697; δ_H (400 MHz, $CDCl_3$) 1.97–2.03 (1H, m, H-2a), 2.08 (1H, dd, $J_{2b,1}$=12.1 Hz, $J_{2b,2a}$=11.4 Hz, H-2b), 3.54 (1H, ddd, $J_{3,4}$=2.5 Hz, $J_{3,2a}$=4.6 Hz, $J_{3,2b}$=10.1 Hz, H-3), 3.55–3.60 (1H, m, H-5), 3.60–3.65 (2H, m, H-6a, H-6b), 3.85 (1H, br s, H-4), 4.42 and 4.48 (2H, 2d, *J*=11.8 Hz, PhCH_2), 4.54–4.66 (4H, m, 3×PhC*H*H, H-1), 4.92 (1H, d, *J*=11.7 Hz, PhCH*H*), 7.22–7.42 (15H, m, 15×C*H* arom.); δ_C (100 MHz, $CDCl_3$) δ 22.1 (C-2), 68.5 (CH_2), 70.4 (CH_2), 71.5 (C-4), 73.6 (CH_2), 74.3 (CH_2), 76.2 (C-5), 77.0 (C-3), 86.9 (C-1), 127.3, 127.5, 127.76, 127.79, 127.9, 128.1, 128.2, 128.4, 128.5, 137.9, 138.0, 138.6; HRFABMS: *m*/*z* calcd for $[C_{27}H_{29}N_3O_4-H]^+$: 458.2079; found for $[M-H]^+$: 458.2080.

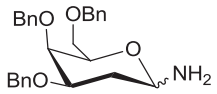
4.43. 1-Amino-3,4,6-tri-*O*-benzyl-2-deoxy-β-D-*arabino*-hexopyranose 8a



3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-*arabino*-hexopyranosyl azide **34a** (1.5 g, 3.27 mmol) was dissolved in methanol (270 mL). Palladium on carbon (10%, 107 mg) was added and the mixture was hydrogenated at atmospheric pressure and room temperature. After 1.5 h the mixture was filtered through Celite to remove the catalyst and the methanol evaporated under reduced pressure to furnish the desired compound **8a** (1.29 g, 91% yield) as a colourless solid.

Mp 97.7 °C (decomp.); $[\alpha]_D^{21}$ 3.3 (*c* 1.7, $CHCl_3$). Found C 74.31, H 7.09, N 3.52. $C_{27}H_{31}O_4N$ requires C 74.80, H 7.20, N 3.20; ν_{max} (film, $CHCl_3$)/cm^{-1} 3387, 3059, 3028, 1955, 1878, 1813, 740, 698; δ_H (400 MHz, $CDCl_3$) 1.42 (1H, ddd, $J_{2a,1}$=10.5 Hz, $J_{2a,3}$=11.6 Hz, $J_{2a,2b}$=12.8 Hz, H-2a), 1.95 (2H, br s, –NH_2), 2.39 (1H, ddd, $J_{2b,1}$=1.8 Hz, $J_{2b,2a}$=12.8 Hz, $J_{2b,3}$=5.0 Hz, H-2b), 2.35–3.54 (2H, m, H-4, H-5), 3.58–3.72 (3H, m, H-3, H-6a, H-6b), 4.17 (1H, dd, $J_{1,2a}$=10.5 Hz, $J_{1,2b}$=1.8 Hz, H-1), 4.49 and 4.89 (2H, 2d, *J*=10.8 Hz, PhCH_2), 4.54 and 4.61 (2H, 2d, *J*=12.2 Hz, PhCH_2), 4.56 and 4.68 (2H, 2d, *J*=11.8 Hz, PhCH_2), 7.07–7.40 (15×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 38.4 (C-2), 69.4 (C-6), 71.4 (CH_2), 73.5 (CH_2), 74.9 (CH_2), 75.8 (C-5), 78.1 (C-4), 80.3 (C-3), 82.4 (C-1), 127.60, 127.64, 127.7, 127.8, 127.9, 128.0, 128.31, 128.35, 128.41, 138.0, 138.39, 138.41; HRFABMS: *m*/*z* calcd for $[C_{27}H_{31}NO_4-H]^+$ 432.2174; found for $[M-H]^+$: 432.2175.

4.44. 1-Amino-3,4,6-tri-*O*-benzyl-2-deoxy-D-*lyxo*-hexopyranose 8b



A solution of 3,4,6-tri-*O*-benzyl-2-deoxy-β-D-*lyxo*-hexoopyranosyl azide **34b** (1.5 g, 3.27 mmol) in methanol (270 mL) containing 10% palladium on carbon (107 mg) was hydrogenated at atmospheric pressure and room temperature. After 1.5 h the mixture was filtered through Celite to remove the catalyst and the methanol evaporated under reduced pressure to furnish the amine **8b** (1.32 g, 93% yield) as a colourless oil and a mixture of anomers (α/β ~ 1:3).

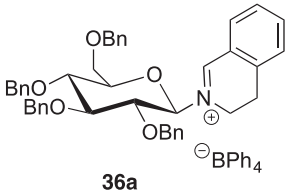
$[\alpha]_D^{22}$ 66.3 (*c* 1.6, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3387, 3059, 3028, 1955, 1878, 1813, 740, 698; δ_H (400 MHz, $CDCl_3$) 1.85 (1H, dd, $J_{2a,1}$=12.0 Hz, $J_{2a,2b}$=11.4 Hz, H-2aβ), 1.95–2.20 (4H, m, −NH_2α, −NH_2β), 2.20–2.32 (3H, m, H-2aα, H-2bα, H-2bβ), 3.41–3.72 (9H, m, H-3β, H-4α, H-4β, H-5α, H-5β, H-6aα, H-6aβ, H-6bα, H-6bβ), 3.78–3.79 (1H, d, $J_{1,2}$=12.0 Hz, H-1β), 4.42 (1H, t, $J_{3,2}$=$J_{3,4}$=3.0 Hz, H-3α), 4.48–4.65 (11H, m, 5×PhC*H*Hβ, 5×PhC*H*Hα, H-1α), 4.91–4.94 (2H, m, PhC*H*Hβ, PhC*H*Hα), 7.14–7.42 (30H, m, 15×C*H*α arom., 15×C*H*β arom.); δ_C (100 MHz, $CDCl_3$) 33.4 (C-2α), 34.2 (C-2β), 69.7 (C-6α), 70.1 (C-6β), 70.2 (*C*H_2α, *C*H_2β), 71.8 (C-5β), 73.4 (*C*H_2α), 73.5 (*C*H_2β), 74.2(*C*H_2α, *C*H_2β), 74.9 (*C*Hα, *C*Hβ), 77.0 (*C*Hα), 77.3 (*C*Hβ), 77.4 (*C*Hα), 83.0 (C-1β), 83.9 (C-1α), 127.26, 127.30, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 138.0, 138.3, 138.8 (3×C quat., arom.); HRFABMS: *m*/*z* calcd for $[C_{27}H_{31}NO_4-H]^+$ 432.2174; found for $[M-H]^+$: 432.2178.

4.45. 2-(2-Bromoethyl)benzaldehyde[55]

Bromine was slowly added over 5 min to an ice cooled solution of isochroman (5 g, 37 mmol) in carbon tetrachloride (20 mL), with stirring at room temperature. After the vigorous reaction had subsided, the cooling bath was removed and the dark brown solution was heated to reflux until the reaction mixture became pale yellow, and liberation of hydrogen bromide gas had ceased. The solution was allowed to reach ambient temperature and the solvent removed in vacuo. Aqueous hydrobromic acid (48%, 7.5 mL) was added to the yellow oily 1-bromoisochroman obtained, and the reaction mixture again heated to reflux. After 10–15 min, the solution was allowed to cool, and extracted with diethyl ether. The organic extracts were washed with water and with dilute sodium hydrogen carbonate, and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure furnished the crude product. Vacuum distillation (ca. 100 °C, 0.5 mbar) yielded the pure product (5.6 g, 72%) as a yellow oil.

ν_{max}/cm^{-1} (neat) 2742, 1697, 1600, 1575, 1260, 1193, 755; δ_H (400 MHz, $CDCl_3$) 3.54–3.63 (4H, m, Ph(CH_2)$_2$Br), 7.33 (1H, d, *J* 7.9 Hz, CH arom), 7.48 (1H, t, *J* 7.9 Hz, C*H* arom.), 7.54 (1H, t, J 7.9 Hz, C*H* arom), 7.8 (1H, d, *J* 7.9 Hz, CH arom.), 10.14 (1H, s, C*H*O); δ_C (100 MHz, $CDCl_3$) 33.2, 36.7, 128.1, 134.1, 134.3, 134.9, 135.2, 140.9, 193.5.

4.46. 2-(1-(2,3,4,6-Tetra-*O*-benzyl-1-deoxy-β-D-glucopyranosyl))-3,4-dihydroisoquinolinium tetraphenylborate 36a

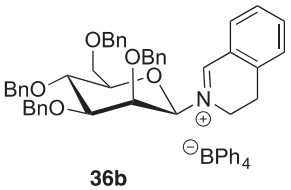


36a

Prepared using general procedure D using 1-amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-glucopyranose **3a** (0.37 g, 0.69 mmol, 1 equiv) and 2-(2-bromoethyl)benzaldehyde (0.16 g, 0.76 mmol, 1.1 equiv) to afford the title compound **36a** as a yellow powder (0.21 g, 31%)

Mp 199–204 °C (decomp.); $[\alpha]_D^{20}$ −14.3 (*c* 1.7, $CHCl_3$); ν_{max} (film, CH_2Cl_2)/cm^{-1}, 3529, 3033, 1952, 1881, 1820, 1719, 1642, 1605, 1573, 1479, 1261; δ_H (400 MHz, $(CD_3)_2CO$) 2.63–2.73 (1H, m, ArC*H*aHb), 2.92–3.11 (1H, m, ArCHa*H*b), 3.26–3.38 (1H, m, C*H*aHbN), 3.59–3.70 (1H, m, CHa*H*bN), 3.75–3.92 (3H, m, C*H*, H-6a, H-6b), 4.05–4.15 (2H, m, 2×C*H*), 4.53–4.82 (5H, m, C*H*, 4×PhC*H*H), 4.91 and 5.03 (2H, 2d, *J* 11.6 Hz, PhCH_2), 4.99 (1H, d, *J* 11.0 Hz, PhC*H*H), 5.04 (1H, d, *J* 11.7 Hz, PhC*H*H), 5.17 (1H, br s, H-1), 6.84 (4H, t, *J* 6.4 Hz, 4×C*H* arom., *ortho* in BPh_4 gp), 7.00 (8H, t, *J* 7.4 Hz, 8×C*H* arom., *meta* in BPh_4 gp), 7.10–7.19 (3H, m, 3×C*H* arom.), 7.24–7.47 (24H, m, 24×C*H* arom.), 7.47–7.56 (3H, m, 3×C*H* arom.), 7.74–7.82 (2H, m, 2×C*H* arom.), 8.95 (1H, s, *H*C=N); δ_C (100 MHz, $(CD_3)_2CO$) 25.3, 47.9, 69.8, 72.5, 73.4, 73.9, 74.6, 75.6, 75.8, 79.3, 83.6, 90.8, 122.5, 125.0, 126.2, 128.27, 128.31, 128.5, 128.6, 129.0, 129.10, 129.15, 129.2, 129.3, 129.5, 135.8, 137.1, 139.1, 139.36, 139.44, 139.8, 139.9, 165.0, 166.3; *m*/*z* calcd for $[C_{43}H_{44}O_5N]^+$: 654.3219; found for iminium cation: 654.3217.

4.47. 2-(1-(2,3,4,6-Tetra-*O*-benzyl-1-deoxy-β-D-mannopyranosyl))-3,4-dihydroisoquinolinium tetraphenylborate 36b

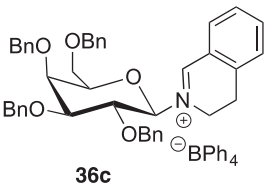


36b

Prepared using general procedure D using 1-amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-mannopyranose **3b** (0.32 g, 0.59 mmol, 1 equiv) and 2-(2-bromoethyl)benzaldehyde (0.14 g, 0.65 mmol, 1.1 equiv) to afford the title compound **36b** as a yellow powder (0.43 g, 75%)

Mp 169.2 °C (decomp.); $[\alpha]_D^{20}$ 16.6 (*c* 1.7, $CHCl_3$); ν_{max} (film, CH_2Cl_2)/cm^{-1} 3052, 2871, 1953, 1881, 1817, 1644, 1604, 1576, 1741, 1453, 1424, 1361, 1316, 1264, 1225, 1095, 1028, 915, 846, 737, 704, 610; δ_H (400 MHz, $(CD_3)_2CO$) 2.69–2.81 (1H, m, ArC*H*aHb), 2.90–3.08 (1H, m, ArCHa*H*b), 3.28–3.29 (1H, m, C*H*aHbN), 3.66–3.81 (2H, m, H-6a, H-6b), 4.00 (1H, dd, *J*=7.6, 15.0 Hz, CHa*H*bN), 4.04–4.13 (2H, m, H-4, H-5), 4.15 (1H, t, *J* 9.0 Hz, H-2), 4.33 (1H, d, *J* 1.6 Hz, H-3), 4.45–4.65 (2H, m, 2×PhC*H*H), 4.74 (1H, m, PhC*H*H), 4.84 (1H, d, *J* 11.8 Hz, PhC*H*H), 4.97(1H, d, *J* 11.7 Hz, PhC*H*H), 4.99 (1H, d, *J* 11.8 Hz, PhC*H*H), 5.03–5.10 (3H, m, PhCH_2, H-1), 6.84 (4H, t, *J*=7.2 Hz, 4×C*H* arom., *para* in BPh_4 gp), 6.98 (8H, t, *J* 7.4 Hz, 8×C*H* arom., *meta* in BPh_4 gp), 7.02–7.07 (1H, m, C*H* arom.), 7.08–7.17 (3H, m, 3×C*H* arom.), 7.20–7.50 (23H, m, 32×C*H* arom.), 7.50–7.57 (3H, m, 3×C*H* arom.), 7.69 (1H, d, *J* 7.0 Hz, C*H* arom.), 7.84 (1H, t, *J* 7.5 Hz, C*H* arom.), 8.77 (1H, s, *H*C=N); δ_C (100 MHz, $(CD_3)_2CO$) 25.3, 44.6, 69.4, 72.8, 73.9, 74.2, 74.8, 75.5, 75.7, 77.4, 83.8, 95.1, 122.4, 124.9, 128.3, 128.4, 128.5, 128.71, 128.73, 128.9, 128.97, 129.04, 129.2, 129.3, 129.40, 129.44, 129.6, 136.1, 137.1, 138.4, 139.10, 139.18, 139.22, 139.7, 165.0, 168.2; *m*/*z* calcd for $[C_{43}H_{44}O_5N]^+$: 654.3219; found for iminium cation: 654.3222.

4.48. 2-(1-(2,3,4,6-Tetra-*O*-benzyl-1-deoxy-β-D-galactopyranosyl))-3,4-dihydroisoquinolinium tetraphenylborate 36c

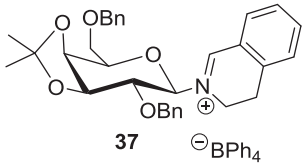


36c

Prepared using general procedure D using 1-amino-2,3,4,6-tetra-*O*-benzyl-1-deoxy-D-galactopyranose **3c** (0.87 g, 1.61 mmol, 1 equiv) and 2-(2-bromoethyl)benzaldehyde (0.38 g, 1.77 mmol, 1.1 equiv) to afford the title compound **36b** as a yellow powder (1.18 g, 75%).

Mp 184–190 °C (decomp.); $[\alpha]_D^{20}$ −9.10 (*c* 1.7, $CHCl_3$); ν_{max} (film, CH_2Cl_2)/cm^{-1} 3053, 2877, 1953, 1881, 1817, 1685, 1613, 1592, 1548, 1477, 1454, 1427, 1364, 1326, 1264, 1212, 1098, 1063, 1029, 912, 868, 821, 737, 703, 610; δ_H (400 MHz, $(CD_3)_2CO$) β anomer 2.83–2.95 (1H, m, ArC*H*aHb), 3.02–3.14 (1H, m, ArCHa*H*b), 3.60–3.75 (1H, m, C*H*aHbN), 3.81–3.94 (4H, m, H-3, H-4, H-6a, H-6b), 4.06–4.048 (2H, m, H-2, H-5), 4.06–4.15 (1H, m, CHa*H*bN), 4.67–4.69 (1H, m, PhC*H*H), 4.75 (1H, d, *J*=10.9 Hz, PhC*H*H), 4.93 (4H, m, 2×PhCH_2), 4.99 (1H, d, *J*=11.2 Hz, PhC*H*H), 5.05 (1H, d, *J* 11.2 Hz, PhC*H*H), 5.23 (1H, d, *J* 8.2 Hz, H-1), 6.81 (4H, t, *J* 7.1 Hz, 4×C*H* arom., *para* in BPh_4 gp), 6.96 (8H, t, *J* 7.4 Hz, 8×C*H* arom., *meta* in BPh_4 gp), 6.99–7.06 (2H, m, 2×C*H* arom.), 7.08–7.16 (3H, m, 3×C*H* arom.), 7.22–7.48 (24H, m, 24×C*H* arom.), 7.58 (1H, t, *J* 7.8 Hz, C*H*), 7.78 (1H, d, *J* 1.0, 7.6 Hz, C*H*), 7.86 (1H, dt, *J* 7.6 Hz, C*H*), 8.98 (1H, s, *H*C=N); δ_C (100 MHz, $(CD_3)_2CO$) 25.4, 44.9, 69.2, 73.9, 75.5, 75.6, 76.2, 78.0, 78.3, 78.8, 86.0, 94.6, 122.4, 124.9, 126.1, 128.5, 128.6, 128.7, 128.8, 129.0, 129.2, 129.3, 129.4, 129.5, 136.2, 137.1, 138.3, 139.1, 139.2, 139.3, 140.4, 165.0, 168.5; *m*/*z* calcd for $[C_{43}H_{44}O_5N]^+$: 654.3219; found for iminium cation: 654.3221.

4.49. 2-[2,6-Di-*O*-benzyl-3,4-*O*-isopropylidene-1-deoxy-D-galactopyranoside]-3,4-dihydroisoquinolinium tetraphenylborate 37

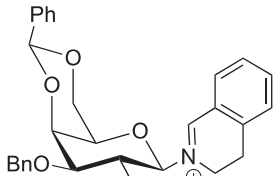


37 $\ominus BPh_4$

Prepared using general procedure D using 1-amino-2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-D-galactopyranoside **4** (1.09 g, 2.73 mmol, 1 equiv) and 2-(2-bromoethyl)benzaldehyde (0.64 g, 3.00 mmol, 1.1 equiv) to afford the title compound **37** as a light brown powder (0.90 g, 43%) and a mixture of anomers (α/β 1:2 by ^1H NMR).

Mp 150–153 °C (decomp.); $[\alpha]_D^{22}$ 91.9 (*c* 1.0, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 3529, 3033, 1952, 1881, 1820, 1719, 1642, 1605, 1573, 1479, 1261; δ_H (400 MHz, $(CD_3)_2CO$) 1.33 (CH_3), 1.42 (CH_3), 3.05–3.18 (1H, m, ArC*H*aHb *isoq-4a*), 2.76–2.79 (1H, m, ArCHa*H*b *isoq-4b*), 3.51–3.63 (1H, m, C*H*aHbN *isoq-3a*), 3.64–3.74 (1H, m, H-6a), 3.77–3.94 (2H, m, CHa*H*bN *isoq-3a*, H-6b), 4.41–4.71 (3H, m, H-2, H-4, H-5); 4.85 (1H, d, *J*=11.6 Hz, PhC*H*H), 4.87–4.98 (3H, m, 3×C*H*), 5.00 (1H, d, $J_{3,4}$=5.8 Hz, H-3), 5.73 (1H, s, H-1), 6.75 (4H, t, *J*=7.2 Hz, 4×C*H* arom., in BPh_4 gp), 6.93 (4H, t, 4×C*H* arom., in BPh_4 gp), 7.09–7.49 (26H, m, 18×C*H* arom., in Ph gp, 8×C*H* arom., in BPh_4 gp), 7.81 (1H, t, *J*=2.1 Hz, C*H* arom.), 9.52 (1H, s, *H*C=N); δ_C (100 MHz, $(CD_3)_2CO$) 24.9 (CH_3), 25.8 (CH_2), 26.9 (CH_3), 46.8 (CH_2), 70.8 (C-5), 71.2 (C-3), 72.1 (C-2), 73.2 (C-4), 73.9 (CH_2), 74.6 (CH_2), 74.7 (C-3), 89.2 (C-1), 111.1 (*C* quat.), 125.3, 122.1, 126.2, 127.12–129.78 (range quoted due to a mixture of anomers, impossible to differentiate between aromatic *C*H signals for each individual isomer in this range), 138.3, 138.5, 139.3, 139.9 (*C*H), 165.3, 165.4 (HC=CN); HRESMS: *m*/*z* calcd for $[C_{32}H_{36}NO_5]^+$ requires 514.2588; found for iminium cation: 514.2591.

4.50. 2-(1-(2,6-Di-*O*-benzyl-3,4-*O*-isopropylidene-1-deoxy-D-galactopyranosyl))-3,4-dihydroisoquinolinium tetraphenylborate 38

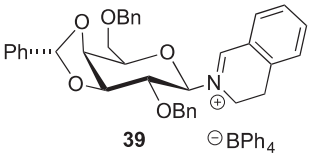


38 $\ominus BPh_4$

Prepared using general procedure D using 1-amino-2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-deoxy-β-D-galactopyranose **5** (1.10 g, 2.23 mmol, 1 equiv) and 2-(2-bromoethyl)benzaldehyde (0.52 g, 2.45 mmol, 1.1 equiv) to afford the title compound **38** as a light brown powder (0.92 g, 47%).

Mp 243–247 °C (decomp.); $[\alpha]_D^{22}$ −21.6 (*c* 1.7, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 3053, 3032, 1952, 1885, 1820, 1642, 1603, 1571, 1452, 1424, 1265, 735, 705; δ_H (400 MHz, $(CD_3)_2SO$) 2.99–3.26 (2H, m, Ar-C*H*aHb *Isoq-4a*, Ar-CHa*H*b *isoq-4b*), 3.78–3.91 (1H, m, C*H*aHbN *Isoq-3a*), 3.95–4.22 (6H, m, CHa*H*bN *isoq-3b*, H-2, H-3, H-5, H-6a, H-6b), 4.61 (1H, d, *J*=11.6 Hz, PhC*H*H), 4.63–4.72 (2H, m, PhC*H*H, H-4), 4.78–4.90 (2H, m, PhCH_2), 5.43 (1H, d, $J_{1,2}$=8.4 Hz, H-1), 5.75 (1H, s, PhC*H*$(O)_2$), 6.79 (4H, t, *J*=7.2 Hz, 4×C*H* arom., *ortho* in BPh_4 gp), 6.93 (8H, t, *J*=7.4 Hz, 8×C*H* arom., *meta* in BPh_4 gp), 7.02–7.63 (25H, m, 25×C*H* arom.), 7.87–7.99 (2H, m, 2×C*H* arom.), 9.407 (1H, s, *H*C=N, *isoq-1*); δ_C (100 MHz, $(CD_3)_2SO$) 24.2 (CH_2 *isoq*-4), 42.9 (CH_2 *isoq*-3), 68.0 (CH_2), 68.57 (C-5), 69.58 (CH_2), 71.4 (C-4), 73.3 (C-2), 74.2 (CH_2), 79.0 (C-3), 93.1 (C-1), 100.2 (PhC*H*$(O)_2$), 121.3, 123.9, 125.2, 134.4, 125.2, 125.3, 126.1, 127.5, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3, 135.4, 137.5, 137.9, 138.06, 138.08, 138.9, 163.78, 167.81 (H*C*=N. *Isoq-1*); *m*/*z* calcd for $[C_{36}H_{36}NO_5]^+$: 562.2593; found for iminium cation: 562.2588.

4.51. 2-(1-(2,6-Di-*O*-benzyl-*endo*-3,4-*O*-benzylidene-1-deoxy-D-galactopyranosyl))-3,4-dihydroisoquinolinium tetraphenylborate 39



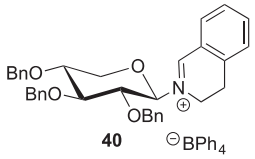
39 $\ominus BPh_4$

Prepared using general procedure D using 1-amino-2,6-di-*O*-benzyl-3,4-*O*-benzylidene-1-deoxy-D-galactopyranose **6** (1.4 g, 3.18 mmol, 1 equiv) and 2-(2-bromoethyl)benzaldehyde (0.75 g, 3.50 mmol, 1.1 equiv) to afford the title compound **39** (1.76 g, 63%) as a yellow crystalline powder and a mixture of anomers (α/β ~ 2.7:1).

Mp 217.1–218.3 °C (dec); $[\alpha]_D^{21}$ 6.5 (*c* 1.0, $CHCl_3$); ν_{max} (film, $CHCl_3$)/cm^{-1} 3053, 3035, 1953, 1890, 1825, 1648, 1604, 1494, 1479, 1402, 1194, 734, 706; δ_H (400 MHz, $(CD_3)_2CO$) 2.78–3.12 (4H, m, ArC*H*aHbα, ArC*H*aHbβ, ArCHa*H*bNα, ArCHa*H*bNβ), 3.54–3.66 (1H, m, C*H*aHbNα), 3.80–4.11 (8H, m, C*H*aHbNβ, CHa*H*bNα, CHa*H*bNβ, H-6aβ, H-6aα, H-6bβ, H-6bα, C*H*α), 4.53–4.58 (2H, m, 2×C*H*β), 4.60–4.69 (7H, m, PhCH_2β, PhCH_2α, C*H*β, 2×C*H*α), 4.74 (1H, t, *J* 5.4 Hz, C*H*β), 4.85 (1H, d, *J* 12.2 Hz, PhC*H*Hβ), 4.86 (1H, d, *J* 11.6 Hz, PhC*H*Hα), 4.99 (1H, dd, *J* 3.0, 8.0 Hz, C*H*α), 5.26 (1H, d, *J* 7.6 Hz, H-1β), 5.86 (1H, d, *J* 3.6 Hz, H-1α), 5.87 (1H, s, C*H*$(O)_2$α), 5.98 (1H, s, C*H*$(O)_2$β), 6.77 (8H, t, *J* 7.2 Hz, 4×C*H*α arom *para* in BPh_4 gp, 4×C*H*β *para* in BPh_4 gp), 6.93 (16H, t, *J* 7.5 Hz, 8×C*H*α arom *meta* in BPh_4 gp, 8×C*H*β arom *meta* in BPh_4 gp), 7.02–7.58 (52H, m, 26×C*H*α arom,

26×C*H*β arom), 7.74–7.81 (2H, m, C*H*α arom, C*H*β arom), 8.88 (1H, s, *H*C=Nβ), 9.17 (1H, s, *H*C=Nα); δ_C (100 MHz, $(CD_3)_2CO$) 25.3, 46.0, 46.3, 69.7, 70.3, 71.1, 71.8, 72.9, 73.3, 73.7, 73.8, 74.2, 74.4, 75.2, 76.2, 76.3, 78.0, 89.5, 92.7, 105.0, 105.5, 122.3, 126.05, 126.08, 126.11, 126.13, 128.0, 128.6, 128.9, 129.12, 129.15, 129.21, 129.24, 129.26, 129.29, 129.36, 129.38, 136.97, 136.99, 139.4, 164.2, 164.7, 164.8, 165.2, 165.7, 167.3; *m*/*z* calcd for $[C_{36}H_{36}NO_5]^+$ 562.2593; found for iminium cation: 562.2594.

4.52. 2-(1-(2,3,4-Tri-*O*-benzyl-1-deoxy-D-xylosyl)-3,4-dihydroisoquinolinium) tetraphenylborate 40



Prepared using general procedure D using 1-amino-2,3,4-tri-*O*-benzyl-D-xylose **7** (1.72 g, 4.12 mmol, 1 equiv) and 2-(2-bromoethyl)benzaldehyde (0.97 g, 4.53 mmol, 1.1 equiv) to afford the title compound **40** (1.2 g, 35%) as a yellow powder and a mixture of anomers (α/β ~ 1:5)

Mp 89–91 °C (decomp.). $[\alpha]_D^{24}$ −36.7 (*c* 1.0, acetone); ν_{max} (film, $CHCl_3$)/cm^{-1} 3500, 3052, 1634, 1602, 1574, 1263; δ_H (400 MHz, $(CD_3)_2CO$) 3.41–3.52 (2H, m, ArC*H*aHbα, ArC*H*aHbβ), 2.84–2.97 (2H, m, ArCHa*H*bα, ArCHa*H*bβ), 3.72–3.76 (1H, m, C*H*α), 3.77–3.97 (4H, m, CHa*H*bNα, CHa*H*bNβ, H-2β, H-4β), 4.29 (1H, dd, *J* 5.4, 11.5 Hz, H-3β), 4.15 (1H, dd, *J* 2.4, 11.4 Hz, C*H*α), 4.29 (1H, dd, *J* 5.4, 11.5 Hz, H-3β), 4.34–4.40 (1H, m, H-5α), 4.43 (1H, d, *J* 11.5 Hz, PhC*H*Hα), 4.60 (1H, d, *J* 11.8 Hz, PhC*H*Hβ), 4.63 (1H, d, *J* 10.8 Hz, PC*H*Hα), 4.64 (1H, d, *J* 12.2 Hz, PhC*H*Hα), 4.68–4.79 (5H, m, PhCH_2β, 3×PhC*H*Hα), 4.89 (1H, d, *J* 10.2 Hz, PhC*H*Hβ), 4.92 (1H, d, *J* 9.6 Hz, PhC*H*Hβ), 5.00 (1H, d, *J* 8.6 Hz, H-1β), 5.07 (1H, d, *J* 11.2 Hz, PhC*H*Hβ), 6.78 (8H, t, *J* 7.2 Hz, 4×C*H*α arom *para* in BPh_4 gp, 4×C*H*β arom *para* in BPh_4 gp), 6.95 (16H, t, *J* 7.5 Hz, 8×C*H*α arom *meta* in BPh_4 gp, 8×C*H*β arom *meta* in BPh_4 gp), 6.97–2.61 (2H, m, 2×C*H*β arom), 7.21–7.45 (31H, m, 17×C*H*α arom, 14×C*H*β arom), 7.47–7.54 (2H, m, C*H*α arom, C*H*β arom), 7.68 (1H, dd, *J* 1.0, 7.7 Hz, C*H*β arom), 7.78 (1H, t, *J* 7.6 Hz, C*H*β arom), 7.94 (1H, dd, *J* 1.1, 6.5 Hz, C*H*α arom), 8.79 (1H, s, *H*C=Nβ), 9.04 (1H, s, *H*C=Nα); δ_C (100 MHz, $(CD_3)_2CO$) 25.2, 25.3, 44.8, 47.3, 66.9, 68.1, 71.9, 72.1, 72.2, 72.6, 73.1, 73.2, 73.4, 75.4, 75.9, 77.3, 77.8, 85.1, 90.3, 94.9, 122.3, 124.7, 125.1, 126.08, 126.11, 126.14, 126.16, 128.4, 128.49, 128.55, 128.60, 128.7, 128.80, 128.84, 129.0, 129.10, 129.15, 129.17, 129.20, 129.3, 129.4, 133.2, 135.6, 136.0, 136.9, 137.0, 138.3, 138.5, 138.7, 139.0, 139.1, 139.2, 139.3, 139.5, 140.2, 164.1, 164.6, 165.1, 165.6, 166.4, 168.3; *m*/*z* calcd for $[C_{35}H_{36}O_4N]^+$: 534.2644; found for iminium cation: 534.2639.

4.53. General procedure for the catalytic asymmetric epoxidation of simple alkenes mediated by iminium salts under aqueous conditions

(a) Using methylstilbene as the substrate

To an ice cooled solution of sodium carbonate (4 equiv) in water (12 mL per 1.5 g of sodium carbonate), Oxone (2 equiv) was added with stirring and the resulting foaming solution was allowed to stir for 5–10 min, so that most of the initial effervescence subsided. The alkene substrate (1 equiv, 100 mol %) was then added as a solution in acetonitrile (6 mL per 1.5 g of sodium carbonate used), followed by the iminium salt (10 mol % with respect to the substrate), also as a solution in acetonitrile of the same volume as the solution of the sodium carbonate. The suspension was stirred at the same temperature for 10 min after which time another equivalent of Oxone was added in four portions over 30 min. The reaction mixture was then left to stir at 0 °C until the substrate was completely consumed by TLC. Work-up and purification were then performed as in the general method.

(b) Using triphenylethylene as the substrate

To an ice cooled solution of sodium carbonate (4 equiv), in water (12 mL per 1.5 g of sodium carbonate), Oxone (2 equiv) was added with stirring and the resulting foaming solution was allowed to stir for 5–10 min so that most of the initial effervescence subsided. The alkene substrate (1 equiv, 100 mol %) was then added as a solution in acetonitrile (6 mL per 1.5 g of sodium carbonate used) followed by the iminium salt (10 mol % with respect to the substrate), also as a solution in acetonitrile of the same volume as the solution of the sodium carbonate. The suspension was then stirred at the same temperature for 10 min after which time another 2.5 equiv of Oxone was added in four portions over 30 min. The reaction mixture was then allowed to stir at 0 °C until the substrate was completely consumed by TLC. Work-up and purification was then performed as in the general method.

(c) Using 1-phenylcyclohexene as the substrate

To an ice cooled solution of sodium carbonate (4 equiv) in water (12 mL per 1.5 g of sodium carbonate), Oxone (2 equiv) was added with stirring and the resulting foaming solution was left to stir for 5–10 min, so that most of the initial effervescence subsided. The alkene substrate (1 equiv, 100 mol %) was then added as a solution in acetonitrile (6 mL per 1.5 g of sodium carbonate used), followed by the iminium salt (10 mol % with respect to the substrate), also as a solution in acetonitrile of the same volume as the solution of the sodium carbonate. The suspension was then stirred at the same temperature until the reaction reached completion by TLC. Work-up and purification were then performed as in the general method.

4.53.1. 1-Phenylcylohexene oxide.[56] ν_{max} (film, $CHCl_3$)/cm^{-1} 3082, 1601, 1492, 1446, 1361, 1250, 1081, 993, 974; δ_H (400 MHz, $CDCl_3$) 1.25–1.39 (1H, m, C*H*H), 1.43–1.72 (4H, m, 2×CH_2), 2.10 (1H, m, C*H*H), 2.28–2.39 (1H, m, C*H*H), 3.07 (1H, s, Ph*H*CO), 7.24–7.28 (1H, m, C*H* arom.), 7.31–7.40 (5H, m, 5×C*H*, arom.); δ_C (100 MHz, $CDCl_3$) 19.81, 20.13, 24.73, 28.86, 37.62, 69.6i, 125.32, 127.17, 128.25, 142.53.

4.53.2. trans-α-Methylstilbene oxide.[56] ν_{max} (film, $CHCl_3$)/cm^{-1} 3059; 1658, 1492, 1449, 1277, 1156, 1065, 980; δ_H (400 MHz, $CDCl_3$) 1.46 (3H, s, CH_3), 3.97 (1H, s, Ph*H*CO), 7.31–7.47 (10H, m, 10×C*H* arom.); δ_C (100 MHz, $CDCl_3$) 16.70, 63.05, 67.09, 125.99, 126.48, 127.50, 127.66, 128.17, 128.32, 128.45, 128.78, 135.93, 142.32.

4.53.3. 2,3,3-Triphenylethylene oxide.[56] ν_{max} (film, $CHCl_3$)/cm^{-1} 3060, 3029, 2955, 2923, 2855, 1602, 1219, 741, 698; δ_H (400 MHz, $CDCl_3$) 4.32 (1H, s, Ph*H*CO), 7.04–7.79 (15H, m, 15×C*H* arom); δ_C (100 MHz, $CDCl_3$) 68.03, 68.6, 126.32, 126.74, 127.54, 127.63, 127.77, 127.83, 127.95, 128.16, 128.61, 135.41, 135.76, 140.96.

4.54. Crystallography

Crystal data for ***25a***: $C_{30}H_{32}O_6$, *M*=488.56, monoclinic, *a*=10.533(5), *b*=8.584(4), *c*=14.241(7) Å, β=94.663(15), *U*=1283.3(11) Å^3, *T*=150(2) K, space group $P2_1$, monochromated Mo Kα radiation, Bruker SMART 1000 CCD diffractometer,[57] λ=0.71073 Å, *Z*=2, D_c=1.264 g cm^{-3}, *F*(000)=520, colourless, dimensions 0.98×0.06×0.06 mm^3, μ=0.087 mm^{-1}, 1.94<θ<27.82°, 7228 reflections measured, 4256 unique, R_{int}=0.0661. The structure was solved by direct methods and refined by full-matrix least-squares[58,59] on F^2. *wR*2=0.2098 (all data, 325 parameters); *R*1=0.0850 [2717 data with $F^2>2\sigma(F^2)$]. *Crystal data for* ***38***:

$C_{63}H_{62}BNO_6$, M=939.95, orthorhombic, a=9.6660(3), b=21.8255(7), c=24.3528(8) Å, U=5137.6(3) Å^3, T=150(2) K, space group $P2_12_12$, Z=4, D_c=1.215 g cm^{-3}, $F(000)$=2000, colourless, dimensions 0.52×0.18×0.14 mm^3, μ=0.077 mm^{-1}, $1.67<\theta<26.00°$, 40,809 reflections measured, 10,074 unique, R_{int}=0.0415, $wR2$=0.0942 (all data, 643 parameters); $R1$=0.0409 [7691 data with $F^2>2\sigma(F^2)$]. Other details as for **25a**. The absolute structures could not be determined reliably from the diffraction data and were set from unchanging chiral centres in the starting materials. Compound **38** contains a diffuse acetone molecule of crystallisation. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 989500 and 989501. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

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