Reactions of N-, S- and O-Nucleophiles with 3,4,6-Tri-O-benzyl-D-glucal Mediated by Triphenylphosphane Hydrobromide versus Those with HY Zeolite

ARTICLE *in* EUROPEAN JOURNAL OF ORGANIC CHEMISTRY · MAY 2006

Impact Factor: 3.07 · DOI: 10.1002/ejoc.200500916

9 AUTHORS, INCLUDING:

Amélia P Rauter
University of Lisbon
117 PUBLICATIONS **1,205** CITATIONS
SEE PROFILE

Tânia Santos Almeida
Universidade Lusófona de Humanidades e …
12 PUBLICATIONS **112** CITATIONS
SEE PROFILE

Ana Vicente
University of Lisbon
7 PUBLICATIONS **62** CITATIONS
SEE PROFILE

M. Guisnet
Université de Poitiers
415 PUBLICATIONS **8,663** CITATIONS
SEE PROFILE

DOI: 10.1002/ejoc.200500916

Reactions of N-, S- and O-Nucleophiles with 3,4,6-Tri-*O*-benzyl-D-glucal Mediated by Triphenylphosphane Hydrobromide versus Those with HY Zeolite

Amélia P. Rauter,*[a] Tânia Almeida,[a] Ana I. Vicente,[a] Verónica Ribeiro,[a] João C. Bordado,[b] João P. Marques,[b] Fernando Ramôa Ribeiro,[b] Maria J. Ferreira,[c] Conceição Oliveira,[c] and Michel Guisnet[d]

Dedicated to Professor András Lipták on the occasion of his 70th birthday

Keywords: Glycosides / Glycosylation / Nucleosides / Rearrangement / Zeolites

Direct C–N bond formation has been accomplished by reaction of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (3,4,6-tri-*O*-benzyl-D-glucal) with N-nucleophiles, using triphenylphosphane hydrobromide as catalyst in dichloromethane or THF. 2-Deoxy-S- and -O-glycosides have also been prepared with thiols, sterols, flavonoids, alcohols and sugars as nucleophiles, with α-stereoselectivity. Sterically demanding reagents such as sterols, flavonoids, sugars and an indole give only the α-anomer in dichloromethane, while the purine nucleosides in THF were obtained as anomeric mixtures whilst maintaining the α-stereoselectivity. This procedure has led to an easy and straightforward synthesis of a variety of biomolecules, in moderate to high yield, with the first use of triphenylphosphane hydrobromide for N- and S-glycosylation. An alternative method for C–O and C–S bond formation uses HY zeolite to promote the Ferrier rearrangement of 3,4,6-tri-*O*-benzyl-D-glucal to give exclusively the corresponding 2,3-unsaturated α-O- and α-S-glycosides in moderate yields.

Introduction

Glycosylation of glycals has been widely used for the synthesis of biologically interesting oligosaccharides and glycoconjugates[1–5] and for the preparation of 2-deoxy glycosides,[6] which are common structural units in many biologically active natural products such as antibiotics[7–10] or cardiac glycosides,[8–11] as well as versatile synthetic intermediates.[12] The synthesis of C-glycosides by palladium-mediated coupling of glycals with suitable aromatic or heterocyclic aglycons has also been reported.[13] Boron trichloride and boron tribromide have been used as catalysts to synthesise silylated 2-deoxy-α-D-O-glycosides in good yields,[14] and the formation of 2-deoxy glycosides catalysed by boron trifluoride etherate depends upon the glycal starting material and the nucleophile.[15] The use of anhydrous sulfonic acid resin,[16] *p*-toluenesulfonic acid[17] and camphorsulfonic acid[18] has also been reported for the preparation of 2-deoxy glycosides. Falck et al.[19] have introduced an O-glycosylation reaction that uses triphenylphosphane hydrobromide (TPHB) as catalyst, in dichloromethane at room temperature, which appears to be unique in its capability to exclusively promote direct addition of oxygen nucleophiles to glucals with α-selectivity using a wide variety of acceptors.[19–23] The dominant anomeric effect contributes to the α-stereoselectivity observed in these reactions. Recently, a polymer-bound diphenylphosphane hydrobromide[24] has been described to promote the synthesis of 2-deoxy glycosides with α-selectivity in high yield. However, allylically rearranged 2,3-unsaturated glycosides were found to be minor products (ca. 10%) in the reaction of 3,4-di-*O*-acetyl-1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol, with octanol and dodecanol catalysed by TPHB in dichloromethane under reflux.[20] Glycosides of this type are also valuable synthetic intermediates for the preparation of deoxy glycosides and constitute the structural units of several antibiotics.[2] A simple route for their synthesis consists of the acid-catalysed reaction of alcohols with glycals, which undergo a Ferrier rearrangement due to the formation of an allyloxycarbenium ion.[25] A diversity of catalysts have been employed in this reaction, including $BF_3{\cdot}Et_2O$,[26] $SnCl_4$,[27] $InCl_3$,[28] $InBr_3$,[29] $Yb(OTf)_3$,[30] $ZnCl_2$,[31]

[a] Departamento de Química e Bioquímica/Centro de Química e Bioquímica, Faculdade de Ciências da Universidade de Lisboa, Ed. C8, 5º Piso, 1749-016 Lisboa, Portugal
Fax: +351-21-7500088
E-mail: aprauter@fc.ul.pt
[b] Centro de Engenharia Biológica e Química, Instituto Superior Técnico,
Av. Rovisco Pais, 1049-001 Lisboa, Portugal
[c] Centro de Química Estrutural, Instituto Superior Técnico,
Av. Rovisco Pais, 1049-001 Lisboa, Portugal
[d] Laboratoire de Catalyse en Chimie Organique, CNRS UMR 6503, Université de Poitiers,
40 Avenue du Recteur Pineau, 86022 Poitiers, France

$LiBF_4$,[32,33] $Sc(OTf)_3$,[34] $BiCl_3$[35] and montmorillonite K-10.[36] Most of the reported Lewis acid catalysed allylic rearrangements have been successful with 3-*O*-acyl protected glycals.[25] Glycal rearrangement of other 3-*O*-protected glycals, however, has only seldom been described, although the rearrangement of 3-*O*-methyl-D-glucal[37] and 3-*O*-benzyl-D-glucal[38], promoted by $BF_3{\cdot}Et_2O$, has been reported. Ceric ammonium nitrate[39] also mediates the Ferrier rearrangement of 3-*O*-benzyl glycals with ethanethiol, although the 2,3-unsaturated products were formed only as minor compounds. Again, the dominant anomeric effect contributes to the α-stereoselectivity observed. However, stereoselective palladium-catalysed O-glycosylation using glycals has also been reported to give Ferrier products[40] in which the anomeric configuration is controlled by the reagent rather than by the anomeric or neighbouring-group effects. Synthesis of 2,3-unsaturated C-glycosides was recently described by reaction of glycals with either organozinc reagents[41] or catalysed by $HClO_4/SiO_2$.[42]

Acid zeolites, which are widely used as catalysts, are microporous crystalline materials that allow environmentally acceptable procedures for the synthesis of fine chemicals.[43–46] Among them, the HY zeolites have been employed in carbohydrate chemistry to promote isomerisation and hydrolysis of disaccharides[47,48] and hydrolysis of methyl glucosides[49] and sucrose.[50] The synthesis of butyl glucopyranosides[51] and glucosylation of alcohols with 1,2-anhydro-α-D-glucopyranose derivatives, catalysed by HY zeolites, have also been reported.[52] The acetonation of various monosaccharides promoted by this solid catalyst favours the formation of the thermodynamically less stable isomers (the furanose derivatives) when D-galactose and L-arabinose are used as starting materials.[53] The reaction with L-sorbose afforded the first synthesis of 1,2-*O*-isopropylidene-α-L-sorbopyranose.[53] These results encouraged the further exploitation of the use of zeolites as promoters of other reactions, namely the reaction of alcohols, flavonoids and thiols with D-glucal. Furthermore, changing over to zeolites instead of using environmentally hazardous catalysts is an additional benefit.

We report herein the first C–N and C–S bond formation using TPHB as catalyst, by reaction of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**1**; 3,4,6-tri-*O*-benzyl-D-glucal) with an indole, purine or thiol to afford the corresponding 2-deoxy nucleosides and 2-deoxy-S-glycosides. This reaction was extended to a variety of O-nucleophiles such as aliphatic alcohols, sterols, sugars and flavonoids. We also undertook the first approach towards the Ferrier rearrangement of **1** mediated by an HY zeolite (FAU topology),[54] which gives exclusively the α-anomer of the 2,3-unsaturated 2,3-dideoxy-O- and -S-glycosides; N-nucleophiles are unreactive with this promoter.

Results and Discussion

Reaction of **1** with octanol, dodecanol and both the thiols in the presence of TPHB afforded the corresponding α- and β-glycosides with different α/β ratios. The α- and β-anomers of the octyl and dodecyl glycosides were isolated in 71% (**2a**), 71% (**3a**), 15% (**2b**) and 16% (**3b**) yields (entries 1 and 2, Table 1). Thioglycosidation with allyl mercaptan and propane-2-thiol, under reflux, gave an inseparable mixture of diastereoisomers **11a** and **11b** (42%) with an α/β ratio of 1:1 and **12a** and **12b** (65%) with an α/β ratio of 2:1; the latter were also formed at 0 °C but in a lower yield (entries 13–15, Table 1). When cholesterol, lanosterol, the racemic flavonoids 6-hydroxyflavanone, 7-hydroxyflavanone and 4-hydroxyflavanone, methyl 2-*O*-benzoyl-4,6-di-*O*-benzylidene-α-D-glucopyranoside and methyl 2,6-di-*O*-pivaloyl-α-D-*ribo*-hexopyranosid-3-ulose were used as nucleophiles, with dichloromethane as solvent, this method was stereoselective and gave only the corresponding α-anomer (entries 3–5, 8, 9, 11, 12, Table 1). Hence, the anomeric stereochemistry, which is due to stereoelectronic effects, may arise from the kinetic anomeric effect expected for trapping the intermediate oxonium ion, and the α/β ratios obtained may be due to differing magnitudes of this effect inherent in the developing C-1-nucleophile bonding.[21] When the reaction of 6-hydroxyflavanone was run in THF at room temperature, only the α-anomer was obtained. However, when running the reaction in THF under reflux the yield and the α-stereoselectivity decreased for the flavanon-6-yl glycoside, and the corresponding β-anomer was detected in low yield (entries 6 and 7, Table 1). The same occurred when 4-hydroxyflavanone was used under the same conditions (entry 10, Table 1). These results contradict those expected when considering the high donor number (DN = 20.0 kcal mol^{-1})[55] and the low polarity[55] of THF. These parameters are both in favour of an increase of the α-selectivity of the reaction, as reported for glycosylation reactions with trichloroacetimidate donors run at low to room temperature in THF and in dichloromethane.[56] The α-directional effect of ethers as solvents is well known and may be due to the interaction of the ether oxygen atom with the sugar oxonium ion intermediate. Their low polarity also contributes to the anomeric outcome, since the anomeric effect is stronger in solvents of low polarity, as confirmed also by the results reported on the glycosylation with thioglycosides as donors at room temperature using dichloromethane and/or ethers as solvents.[57] The explanation for the results obtained may be related to the stability of the oxycarbenium–solvent intermediate, which probably decreases with increasing temperature.

The anomeric configuration of the glycosides was assigned from the NMR spectroscopic data given in the Experimental Section. The HMBC correlations detected for the cholesteryl and lanosteryl glycosides **4** and **5**, respectively, were determinant for their assignment (Table 2), particularly those for carbons C-10′ and C-13′ of compound **4** and C-4′, C-8′, C-9′, C-10′, C-13′ and C-14′ of compound **5**. Due to their stereogenic centre at position 2, the 2′-H resonances of the flavanone glycosides appear as a complex signal, which is consistent with the presence of inseparable α-D-diastereoisomers in dichloromethane for **6a**–**8a** and α,β-D-diastereoisomers in THF under reflux (entries 5–10,

Table 1). Assignment of the quaternary carbon atoms of the flavonoid A ring of compound **7a** was accomplished by considering the HMBC correlations of C-4′a at δ = 162.4 ppm with the multiplet at δ = 6.75–6.70 ppm, which contains the resonances of 6′-H, 8′-H, while C-7′ and C-8a′ were assigned at δ = 163.3 and 163.0 ppm, both of which have correlations with 5′-H at δ = 7.86 ppm. This proton also exhibits an HMBC correlation with C-4′ (carbonyl carbon atom), as expected. For compound **8a**, the C-1′′ signal at δ = 132.0 ppm was confirmed by its HMBC correlation with 3′′-H and 5′′-H at δ = 7.17 ppm, which appears at lower chemical shift than those detected for this carbon atom in the flavonoid glycosides **6a** and **7a** due to the substitution at position 4′′.

Condensation of **1** with 5,6-dimethoxyindole, catalysed by TPHB, was investigated in the presence of solvents with different boiling points and with increasing polarity,[55] such as toluene, THF and dichloromethane, either at room temperature or under reflux (entries 16–19, Table 1). The α-D-nucleoside **13** was isolated in low yield (12–20%) under these reaction conditions, while the β-anomer was not detected by TLC in the reaction mixture. Reaction at C-3 of the indole ring was ruled out by examination of the NMR spectra of compound **13**, which presents the resonances of

Table 1. O-, S-, and N-Glycosylation mediated by TPHB.

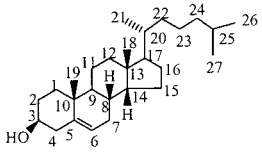
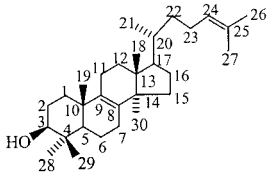
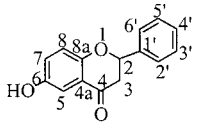
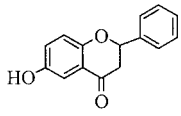
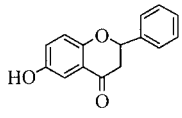
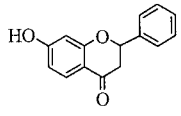
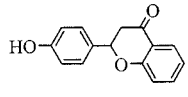
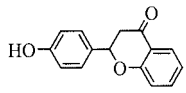
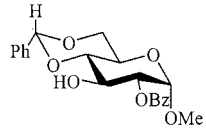
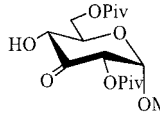
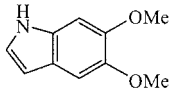
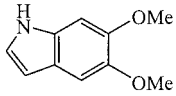
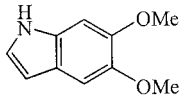
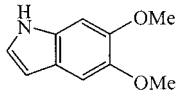
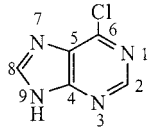
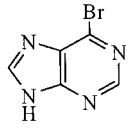
Entry	Nucleophile	Conditions[a]	α/β ratio	Isolated yield (%)
1	$HO(CH_2)_7CH_3$	CH_2Cl_2/reflux/ 50 min	5/1	**2a** (71); **2b** (15)
2	$HO(CH_2)_{11}CH_3$	CH_2Cl_2/reflux/ 50 min	5/1	**3a** (71); **3b** (16)
3		CH_2Cl_2/reflux/ 75 min	100/0	**4** (67)
4		CH_2Cl_2/reflux/ 60 min	100/0	**5** (43)
5		CH_2Cl_2/reflux/ 150 min	100/0	**6a** (54) **1** (21)[b]
6		THF/r.t./ 150 min	100/0	**6a** (25) **1** (32)[b]
7		THF/reflux/ 150 min	5/1	**6a,b** (62) **1** (18)[b]
8		CH_2Cl_2/reflux/ 150 min	100/0	**7a** (70) **1** (14)[b]
9		CH_2Cl_2/reflux/ 150 min	100/0	**8a** (57) **1** (20)[b]

Table 1. *(continued)*.

Entry	Nucleophile	Conditions[a]	α/β ratio	Isolated yield (%)
10		THF/reflux/ 150 min	10/1	**8a,b** (39) **1** (8)[b]
11		CH_2Cl_2/reflux/ 150 min	100/0	**9**(64)
12		CH_2Cl_2/reflux/ 150 min	100/0	**10** (40)
13	$HSCH_2CH{=}CH_2$	CH_2Cl_2/reflux/ 150 min	1/1	**11a,b** (42)
14	$HSCH(CH_3)_2$	CH_2Cl_2/0 °C/ 24 h	2/1	**12a,b** (49)
15	$HSCH(CH_3)_2$	CH_2Cl_2/reflux/ 150 min	2/1	**12a,b** (65)
16		toluene/reflux/ 150 min	100/0	**13** (19) **1** (19)[b]
17		CH_2Cl_2/r.t./ 24 h	100/0	**13** (20) **1** (36)[b]
18		THF /reflux/ 180 min	100/0	**13** (20) **1** (22)[b]
19		CH_2Cl_2/reflux/ 150 min	100/0	**13** (12) **1** (77)[b]
20		THF/reflux/ 180 min	3/1	**14a,b** (39) **1** (26)[b]
21		THF/reflux/ 180 min	3/1	**15a,b** (48) **1** (23)[b]

[a] Conditions: 3,4,6-tri-*O*-Benzyl-D-glucal **1** (1 mmol), nucleophile (2 mmol), TPHB (0.079 mmol). [b] Recovered starting material (%).

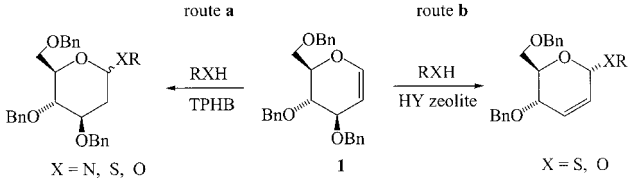
2-H and 3-H at δ = 6.77 and 6.33 ppm, respectively, each as a doublet, and of CH-2 and CH-3 at δ = 123.5 and 102.4 ppm, respectively. The low solubility of 6-chloropurine and 6-bromopurine in dichloromethane hampers their reactivity, therefore THF was used instead. The 2-deoxynucleosides **14a**,**b** and **15a**,**b** were obtained in 39% and 48% isolated yield, respectively, as anomeric mixtures with an α/β ratio of 2:1 and 3:1 (entries 20 and 21, Table 1), the starting material being recovered in 26% and 23% yield, respectively. The reaction is regioselective, and the presence of the N^9-isomers was confirmed by the HMBC correlations of 1′-H with C-8 and C-4, of 8-H with C-4 and C-5 and of 2-H with C-4 and C-6 observed for compounds **14a** and **15a**.

When the reaction was carried out in the presence of the acid zeolite HY, with octanol, 6-hydroxyflavanone and propane-2-thiol as nucleophiles in dichloroethane, the 2,3-unsaturated α-D-glycosides **16**, **17** and **18** were obtained in moderate yields (55–47%; Scheme 1, route b), while in dichloromethane, which has a lower boiling point, the yields were lower (entries 1–4, 9 and 10, Table 3). No reaction was detected when methyl 2-*O*-benzoyl-4,6-di-*O*-benzylidene-α-D-glucopyranoside, methyl 2,6-di-*O*-pivaloyl-α-

Table 2. Relevant HMBC correlations for assignment of NMR data of compounds **4** and **5**.

Carbon atom	^{13}C	HMBC
4		
1′	37.1	m (H-2eq, H-4′ax, H-4′eq), Me-19′
3′	75.9	m (H-2eq, H-4′ax, H-4′eq)
4′	40.0	Me-19′
6′	121.6	m (H-2eq, H-4′ax, H-4′eq)
8′	31.9	H-6′, Me-19′
9′	50.1	Me-19′
10′	36.7	Me-19′
12′	39.8	Me-18′
13′	42.3	Me-18′
14′	56.7	Me-18′
16′	28.2	Me-18′
17′	56.1	Me-18′, Me-21′
22′	36.2	Me-21′
23′	23.8	Me-26′, Me-27′
24′	39.5	Me-26′, Me-27′
25′	28.0	Me-26′, Me-27′
5		
4′	37.4	Me-19′
5′	51.1	Me-28′, Me-29′
8′	134.8	Me-30′
9′	134.9	Me-19′
10′	38.9	Me-28′, Me-29′, H-3′
12′	31.5	Me-18′, Me-30′
13′	50.2	Me-18′, Me-30′, Me-21′
14′	44.9	Me-18′, Me-30′
17′	50.8	Me-18′, Me-30′
23′	36.8	H-21′, Me-26′, Me-27′
28′	1 6.8	H-3′
29′	29.1	H-3′

D-*ribo*-hexopyranosid-3-ulose and 5,6-dimethoxyindole were the nucleophiles used (entries 5–8, 11 and 12, Table 3). The 2,3-unsaturation was confirmed by the signals of C-2, C-3 and 2-H, 3-H. The $^3J_{1,2}$ coupling constant is in agreement with the presence of 1-H equatorially attached to 2,3-unsaturated pyranoid structures,[58] thus indicating that the obtained compounds are α-anomers. The α-configured Ferrier product **17** is an inseparable mixture of 2′*R* and 2′*S* diastereoisomers, as confirmed by the resonances of 2′-H, 3′ax-H, 3′eq-H and 5′-H, which appear as complex signals instead of exhibiting the expected coupling patterns.



Scheme 1.

The Ferrier reaction promoted by the acid zeolite occurs by debenzoxylation at position 3, leading to a highly stabilised allyloxycarbenium ion, which undergoes nucleophilic attack at the anomeric position to afford the α-configured glycoside. This result can be explained on the basis of the HSAB concept. Protonation of the hard C-3 oxygen centre by the zeolite leads to formation of the Ferrier product, while TPHB protonates the softer C-2 enolic centre, as suggested by Falck et al.[19] Treatment of octyl 3,4,6-tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (**2a**) with the acid zeolite under the same reaction conditions but in the absence of octanol did not lead to any reaction products, thus confirming that debenzoxylation only takes place if an allyloxycarbenium ion can be formed, as expected. The shape-selectivity of the zeolite may also influence the selectivity in obtaining exclusively 2,3-unsaturated glycosides over the corresponding 2-deoxy glycosides, due to the possible hindrance of the diffusion of the reagents and the reaction products, or to steric limitations in the formation of the transition state. The mono-esterification of polyols mediated by HY is an example of a shape-selective reaction inside the pores, whose rate and yield depend on the Si/Al ratio.[59]

In the present work, the acid zeolite HY promotes stereoselective O- and S-glycosidation to give exclusively the α-anomer of the Ferrier product. Since most of the available catalysts are successful only with 3-*O*-acyl-protected glycals, the methodology developed should prove to be synthetically useful for the preparation of 2,3-unsaturated glycosides protected with benzyl groups, which are stable in a wide variety of reaction conditions, and may be used for further synthetic approaches that avoid protection/deprotection steps, which diminish the overall reaction yield.

Conclusions

The results obtained for the reaction of 1,5-anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**1**) with N-, S- and O-nucleophiles, in the presence of TPHB or HY zeolite enable the following considerations:

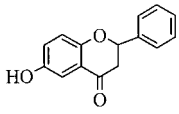
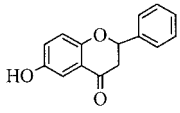
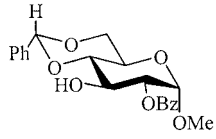
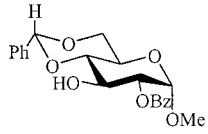
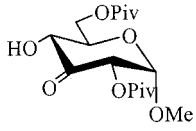
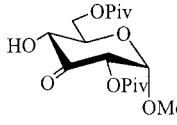
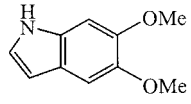
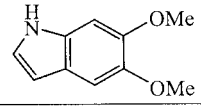
(i) TPHB-catalysed glycosylation is an efficient and straightforward method to link not only a variety of O-nucleophiles to glycals, but also S- and N-nucleophiles, thus affording the corresponding 2-deoxy-O-, -S-glycosides and 2-deoxynucleosides;

(ii) The reaction with aliphatic alcohols, propane-2-thiol and purines is α-stereoselective, giving α/β ratios that depend upon the nucleophile used, while sterically demanding nucleophiles such as sterols, flavonoids and sugars lead exclusively to the corresponding α-glycoside;

(iii) When the reaction with O- and S-nucleophiles is mediated by HY zeolite, only the α-anomer of the Ferrier product is obtained. This new method constitutes a simple experimental procedure that provides a cleaner technology in which the zeolite is easily separated from the reaction media and can therefore be regenerated;

(iv) This approach leads to an easy entry to 2,3-unsaturated O- and S-glycosides and provides a method to transform 3-*O*-benzyl glycals into Ferrier products in moderate yield and expands the synthetic use of the Ferrier rearrangement to benzyl-protected compounds.

Table 3. Ferrier Rearrangement promoted by HY zeolite.

Entry	Nucleophile	Conditions[a]	α/β ratio	Isolated yield (%)
1	$HO(CH_2)_7CH_3$	CH_2Cl_2/reflux	100/0	**16** (47) **1** (3)[b]
2	$HO(CH_2)_7CH_3$	$ClCH_2CH_2Cl$/reflux	100/0	**16** (54) **1** (2)[b]
3		CH_2Cl_2/reflux	100/0	**17** (43) **1** (8)[b]
4		$ClCH_2CH_2Cl$/reflux	100/0	**17** (46) **1** (7)[b]
5		CH_2Cl_2/reflux	–	**1** (100)[b]
6		$ClCH_2CH_2Cl$/reflux	–	**1** (100)[b]
7		CH_2Cl_2/reflux	–	**1** (100)[b]
8		$ClCH_2CH_2Cl$/reflux	–	**1** (100)[b]
9	$HSCH(CH_3)_2$	CH_2Cl_2/reflux	100/0	**18** (46) **1** (4)[b]
10	$HSCH(CH_3)_2$	$ClCH_2CH_2Cl$/reflux	100/0	**18** (55) **1** (2)[b]
11		CH_2Cl_2/reflux	–	**1** (100)[b]
12		$ClCH_2CH_2Cl$/reflux	–	**1** (100)[b]

[a] Conditions: 3,4,6-tri-*O*-Benzyl-D-glucal **1** (1 mmol), nucleophile (2.5 mmol), HY zeolite, 150 min. [b] Recovered starting material (%).

Experimental Section

Zeolite Preparation and Characterisation: The acid form of the zeolite, HY, was prepared by calcination of the corresponding ammonium form, NH_4Y (LZY-82 from Union Carbide), at 500 °C (under dry air flow, 60 mL min^{-1} g^{-1}). The sample was characterised by X-ray powder diffraction and showed a good level of crystallinity. Scanning electron microscopy (SEM) was used to evaluate crystal sizes and morphology; HY presented spherical particles with a diameter of about 1 μm. The surface area and pore size distribution was evaluated by nitrogen adsorption at 77 K; HY presented a BET apparent surface area of 731 m^2 g^{-1}, and a micropore volume and external surface area of 0.30 cm^3 g^{-1} and 15 m^2 g^{-1}, respectively (determined by the t-plot procedure). The global composition was obtained from the elemental chemical analysis, and their framework composition was determined by ^{29}Si and ^{27}Al magic angle spinning nuclear magnetic resonance (MAS NMR); HY presented a framework with a Si/Al ratio of 4.5 and a global Si/Al ratio of 2.7, with a residual sodium content of 2% of the total cationic positions.

The acidity of the HY sample was evaluated by temperature-programmed desorption (TPD) of ammonia. Details of the procedure and the corresponding thermograms can be found in a previous reference.[60]

General: All reactions were monitored by TLC (silica gel 60 F_{254}, Merck) with detection by UV light and/or by vanillin in sulfuric

acid solution (2.5%) spray, followed by heating at 120 °C. Solutions were concentrated on a rotary evaporator under reduced pressure below 40 °C. Column chromatography (CC) was performed on silica gel 60 G (0.040–0.063 mm, E. Merck) and elution under low pressure. Melting points were determined with an Electrothermal 9100 instrument and are uncorrected. ^{1}H and ^{13}C NMR spectra, DEPT, COSY, NOESY, HMQC and HMBC experiments were recorded using the following spectrometers: a BRUKER CPX 300 operating at 300.14 MHz for ^{1}H and 75.43 MHz for ^{13}C, a BRUKER Avance 400 operating at 400.13 MHz for ^{1}H and 100.62 MHz for ^{13}C, and a BRUKER DRX500 operating at 500.13 MHz for ^{1}H and 125.77 MHz for ^{13}C, equipped with a BBI-XYZ probe head (5 mm diameter). All the spectrometers were operating at a constant temperature of 298 K. The solvent used was $CDCl_3$ (1% v/v Me_4Si or 0.03% v/v Me_4Si, Aldrich). IR spectra were recorded with a Hitachi 270-50 spectrometer and UV spectra on a Shimadzu UV-1603 using dichloromethane as solvent. Optical rotations were recorded with a Perkin–Elmer 343 polarimeter. Elemental analyses were performed at the Microanalyses Service of the Instituto Superior Técnico, Universidade Técnica de Lisboa. High resolution mass spectra were obtained with a Finnigan FT/MS 2001 DT, FT-ICR/MS mass spectrometer equipped with a Nd:YAg laser operating at its fundamental wavelength (1064 nm).

Typical Experimental Procedure for the Preparation of 2-Deoxy Glycosides Mediated by TPHB: A solution of the nucleophile (2 mmol) in dry dichloromethane (or THF or toluene when indicated; the lowest volume necessary to dissolve the nucleophile) was added to a solution of **1** (417 mg, 1 mmol) in dichloromethane (or THF or toluene when indicated; 5 mL) and TPHB (27 mg, 0.079 mmol). The mixture was stirred under reflux for 150 min (or as otherwise indicated). After cooling to room temp., CH_2Cl_2 (30 mL) was added to the reaction mixture and the solution washed with a saturated solution of $NaHCO_3$ (20 mL). Evaporation and column chromatography with EtOAc/*n*-hexane or EtOAc/toluene afforded the corresponding 2-deoxy glycosides.

Octyl 3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (2a) and Octyl 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-*arabino*-hexopyranoside (2b): Reaction of **1** with octanol (261 mg, 2 mmol) for 50 min gave **2a** as a syrup (388 mg, 71%) and **2b** also as a syrup (83 mg, 15%).

2a: R_f = 0.49 (EtOAc/*n*-hexane, 1:6). $[\alpha]_D^{20}$ = +23 (c = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1600 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 231 nm (1877). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 7.56–7.20 (m, 15 H, Ph), 4.99–4.91 (m, 2 H, 1-H, part A of AB system, OCH_2Ph), 4.70–4.53 (m, 5 H, OCH_2Ph), 3.81 (ddd, $^3J_{3,4}$ = 9.0, $^3J_{2eq,3}$ = 5.1, $^3J_{2ax,3}$ = 11.1 Hz, 1 H, 3-H), 3.73–3.64 (m, 5 H, 4-H, 5-H, 6_A-H, 6_B-H, $1'_A$-H), 3.38 (dt, $^3J_{1'A,1'B}$ = 9.5, $^3J_{1'B,2'}$ = 6.6 Hz, 1 H, $1'_B$-H), 2.31 (dd, $^2J_{2ax,2eq}$ = 12.9, $^3J_{2eq,3}$ = 5.1 Hz, 1 H, 2eq-H), 1.76 (ddd, $^2J_{2ax,2eq}$ = 12.9, $^3J_{2ax,3}$ = 11.1, $^3J_{1,2ax}$ = 2.8 Hz, 1 H, 2ax-H), 1.61–1.56 (m, 12 H, 2′-H – 7′-H), 0.93 (t, $^3J_{7',8'}$ = 6.6 Hz, 3 H, 8′-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 138.7, 138.5, 138.2 (C_q, Ph), 128.3, 127.8, 127.5 (CH, Ph), 97.3 (C-1), 78.3 (C-4), 77.7 (C-3), 74.9, 73.4, 71.7 (O*C*H$_2$Ph), 70.6 (C-5), 68.9 (C-6), 67.3 (C-1′), 35.5 (C-2), 31.8, 29.3, 26.2, 22.6 (C-2′–C-7′), 14.0 (C-8′) ppm. $C_{35}H_{46}O_5$ (546.74): calcd. C 76.89, H 8.48; found C 76.74, H 8.65.

2b: R_f = 0.54 (EtOAc/*n*-hexane, 1:6). $[\alpha]_D^{20}$ = +5 (c = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1600 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 238 nm (3253). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 7.40–7.23 (m, 15 H, Ph), 4.96, 4.92 (part A of AB system, OCH_2Ph, $^3J_{AB}$ = 12.0 Hz), 4.75–4.58 (m, 5 H, OCH_2Ph), 4.47 (dd, $^3J_{1,2ax}$ = 9.6, $^3J_{1,2eq}$ = 1.5 Hz, 1 H, 1-H), 3.94 (dt, $^2J_{1'A,1'B}$ = 9.3, $^3J_{1'A,2'}$ = 6.6 Hz, 1 H, $1'_A$-H), 3.79–3.75 (m, 3 H, 3-H, 6_A-H, 6_B-H), 3.54–3.46 (m, 3 H, 4-H, 5-H, $1'_B$-H), 2.36 (ddd, $^3J_{1,2eq}$ = 1.5, $^2J_{2eq,2ax}$ = 12.6, $^3J_{2eq,3}$ = 4.8 Hz, 1 H, 2eq-H), 1.75–1.62 (m, 3 H, 2ax-H, 2′-H), 1.32 (br. s, 8 H, 3′-H–7′-H), 0.93 (t, $^3J_{7',8'}$ = 6.9 Hz, 3 H, 8′-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 138.3 (C_q, Ph), 128.4, 128.3, 128.0, 127.7, 127.6, 127.5 (CH, Ph), 99.8 (C-1), 79.5 (C-3), 78.2 (C-4), 75.2 (C-5), 74.9, 73.4, 71.4 (O*C*H$_2$Ph), 69.5, 69.4 (C-6, C-1′), 36.7 (C-2), 31.8, 29.6, 29.4, 29.2, 26.1, 22.6 (C-2′–C-7′), 14.1 (C-8′) ppm. HRMS: calcd. for $C_{35}H_{46}O_5$ 546.334922; found 546.334525.

Dodecyl 3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (3a) and Dodecyl 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-*arabino*-hexopyranoside (3b): Reaction of **1** with dodecanol (381 mg, 2 mmol) for 50 min gave **3a** as a syrup (431 mg, 71%) and **3b** also as a syrup (99.2 mg, 16%).

3a: R_f = 0.63 (EtOAc/*n*-hexane, 1:2). $[\alpha]_D^{20}$ = +52 (c = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1600 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 253 nm (9966), 234 (1026). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 7.39–7.19 (m, 15 H, Ph), 4.97 (d, $^3J_{1,2ax}$ = 2.7 Hz, 1 H, 1-H), 4.94, 4.90 (part A of AB system, $^2J_{AB}$ = 12.0 Hz, 1 H, OCH_2Ph), 4.70–4.66 (m, 3 H, OCH_2Ph), 4.56–4.52 (m, 2 H, OCH_2Ph), 3.80 (ddd, $^3J_{2eq,3}$ = 5.4, $^3J_{2ax,3}$ = 11.4, $^3J_{3,4}$ = 8.9 Hz, 1 H, 3-H), 3.83–3.78 (m, 2 H, 5-H, 6_A-H), 3.71–3.62 (m, 3 H, 4-H, 6_B-H, $1'_A$-H), 3.35 (dt, $^3J_{1'A,1'B}$ = 9.6, $^3J_{1'B,2'}$ = 6.6 Hz, 1 H, $1'_B$-H), 2.28 (dd, $^2J_{2ax,2eq}$ = 12.9, $^3J_{2eq,3}$ =5.4 Hz, 1 H, 2eq-H), 1.74 (ddd, $^3J_{1,2ax}$ = 2.7, $^2J_{2ax,2eq}$ = 12.9, $^3J_{2ax,3}$ = 11.4 Hz, 1 H, 2ax-H), 1.59–1.55 (m, 2 H, 2′-H), 1.29 (br. s, 18 H, 3′-H–11′-H), 0.91 (t, $^3J_{11',12'}$ = 6.6 Hz, 3 H, 12′-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 138.7, 138.5, 138.1 (C_q, Ph), 129.7, 128.9, 128.3, 127.9, 127.8, 127.5, 127.4 (CH, Ph), 97.3 (C-1), 78.3 (C-4), 77.7 (C-3), 74.9, 73.4, 71.7 (O*C*H$_2$Ph), 70.6 (C-5), 68.9 (C-6), 67.4 (C-1′), 35.5 (C-2), 31.9, 29.6, 29.5, 29.4, 29.3, 26.2, 22.6 (C-2′–C-11′), 14.1 (C-12′) ppm. HRMS: calcd. for $C_{39}H_{54}O_5$ 602.397590; found 602.397125.

3b: R_f = 0.73 (EtOAc/*n*-hexane, 1:2). $[\alpha]_D^{20}$ = –3 (c = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1600 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 235 nm (1768). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 7.35–7.19 (m, 15 H, Ph), 4.92, 4.88 (part A of AB system, $^2J_{AB}$ = 12.0 Hz, OCH_2Ph), 4.70–4.53 (m, 5 H, OCH_2Ph), 4.43 (dd, $^3J_{1,2ax}$ = 9.6, $^3J_{1,2eq}$ = 1.8 Hz, 1 H, 1-H), 3.89 (dt, $^2J_{1'A,1'B}$ = 9.9, $^3J_{1'A,2'}$ = 6.9 Hz, 1 H, $1'_A$-H), 3.75–3.67 (m, 3 H, 3-H, 6_A-H, 6_B-H), 3.49–3.41 (m, 3 H, 4-H, 5-H, $1'_B$-H), 2.36 (ddd, $^3J_{1,2eq}$ = 1.8, $^2J_{2eq,2ax}$ = 12.3, $^3J_{2eq,3}$ = 5.1 Hz, 1 H, 2eq-H), 1.70–1.57 (m, 3 H, 2ax-H, 2′-H), 1.25 (br. s, 18 H, 3′-H–11′-H), 0.88 (t, $^3J_{11',12'}$ = 6.0 Hz, 3 H, 12′-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 138.3 (C_q, Ph), 128.3, 127.9, 127.6, 127.4 (CH, Ph), 99.7 (C-1), 79.4 (C-3), 78.1 (C-4), 75.2 (C-5), 74.9, 73.4, 71.3 (O*C*H$_2$Ph), 69.4 (C-6, C-1′), 36.7 (C-2), 31.8, 29.6, 29.4, 29.3, 26.0, 22.6 (C-2′–C-11′), 14.0 (C-12′) ppm. HRMS: calcd. for $C_{39}H_{54}O_5$ 602.397292; found 602.397125.

Cholesteryl 3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (4): Reaction of **1** with cholesterol (774 mg, 2 mmol) for 75 min gave **4** as a white solid (540 mg, 67%); m.p. 122–124 °C; R_f = 0.53 (EtOAc/*n*-hexane, 1:5). $[\alpha]_D^{20}$ = +47 (c = 1.1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1625 cm^{-1} (C=C), 1590 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 259 nm (1843), 230 (1968). ^{1}H NMR (500.13 MHz, $CDCl_3$, 25 °C): δ = 7.45–7.29 (m, 15 H, Ph), 5.41 (br. s, 1 H, 6′-H), 5.26 (br. s, 1 H, 1-H), 5.03, 4.99 (part A of AB system, $^3J_{AB}$ = 10.8 Hz, 1 H, OCH_2Ph), 4.78–4.59 (m, 5 H, OCH_2Ph), 4.15 (ddd, $^3J_{2ax,3}$ = 10.8, $^3J_{2eq,3}$ = 4.0, $^3J_{3,4}$ = 8.0 Hz, 1 H, 3-H), 4.01–3.91 (m, 2 H, 5-H, 6_A-H), 3.82–3.71 (m, 2 H, 4-H, 6_B-H), 3.60–3.57 (m, 1 H, 3′-H), 2.43–2.35 (m, 3 H, 2eq-H, 4′ax-H, 4′eq-H), 1.11 (s, 3 H, 19′-Me), 1.04 (d, $^3J_{20',21'}$ = 6.3 Hz, 3 H, 21′-Me), 0.99 (d, $^3J_{25',Me}$ = 6.0 Hz, 6 H, 26′-Me, 27′-Me), 0.79 (s, 3 H, 18′-Me) ppm. ^{13}C NMR (125.77 MHz, $CDCl_3$, 25 °C): δ = 140.8 (C-5′), 138.8, 138.5, 138.2 (C_q, Ph), 128.3, 127.9, 127.5 (CH, Ph), 121.6 (C-6′), 95.0 (C-1),

78.4 (C-4), 77.8 (C-3), 75.9 (C-3′), 75.0, 73.4, 71.7 (O*C*H$_2$Ph), 70.7 (C-5), 69.0 (C-6), 56.7 (C-14′), 56.1 (C-17′), 50.1 (C-9′), 42.3 (C-13′), 40.0 (C-4′), 39.8 (C-12′), 39.5 (C-24′), 37.1 (C-1′), 36.7 (C-10′), 36.2 (C-22′), 36.0 (C-2), 35.8 (C-20′), 31.9 (C-8′), 28.2 (C-16′), 28.0 (C-25′), 27.7 (C-2′), 24.3 (C-15′), 23.8 (C-23′), 22.8 (C-27′), 22.6 (C-26′), 21.0 (C-19′), 19.3 (C-11′), 18.7 (C-21′), 11.9 (C-18′) ppm. HRMS: calcd. for $C_{54}H_{74}O_5$ 802.553732; found 802.553625.

Lanosteryl 3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (5): Reaction of **1** with lanosterol (853 mg, 2 mmol) for 60 min gave **5** as a syrup (346 mg, 43%); R_f = 0.53 (EtOAc/*n*-hexane, 1:2). $[\alpha]_D^{20}$ = +66 (*c* = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1600 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 247 nm (1843), 230 (1968). ^{1}H NMR (500.13 MHz, $CDCl_3$, 25 °C): δ = 7.47–7.27 (m, 15 H, Ph), 5.26 (d, $^3J_{1,2a}$ = 3.0 Hz, 1 H, 1-H), 5.21 (br. t, $^3J_{23',24'}$ = 6.0 Hz, 1 H, 24′-H), 5.01, 4.97 (part A of AB system, $^2J_{AB}$ = 10.8 Hz, 1 H, OC*H*$_2$Ph), 4.76–4.57 (m, 5 H, OC*H*$_2$Ph), 4.15 (ddd, $^3J_{2ax,3}$ = 11.1, $^3J_{2eq,3}$ = 4.8, $^3J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 4.02 (ddd, $^3J_{4,5}$ = 10.2, $^3J_{5,6A}$ = 3.6, $^3J_{5,6B}$ = 1.8 Hz, 1 H, 5-H), 3.88 (dd, $^3J_{5,6A}$ = 3.6, $^2J_{6A,6B}$ = 10.5 Hz, 1 H, 6$_A$-H), 3.76–3.68 (m, 2 H, 4-H, 6$_B$-H), 3.22 (dd, $^3J_{2'A,3'}$ = 3.3, $^3J_{2'B,3'}$ = 11.1 Hz, 1 H, 3′-H), 2.27 (dd, $^2J_{2ax,2eq}$ = 12.3, $^3J_{2eq,3}$ = 4.8 Hz, 1 H, 2eq-H), 1.68, 1.60 (each s, 3 H, 26′-H, 27′-H), 0.98 (s, 3 H, 19′-H), 0.96, 0.80 (each s, 3 H, 28′-H, 29′-H), 0.92 (d, $^3J_{20',21'}$ = 7.0 Hz, 3 H, 21′-H), 0.88 (s, 3 H, 30-H), 0.69 (s, 3 H, 18′-H) ppm. ^{13}C NMR (125.77 MHz, $CDCl_3$, 25 °C): δ = 139.2, 139.0, 138.7 (Cq, Ph), 134.9 (C-9′), 134.8 (C-8′), 131.3 (C-25′), 130.2, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9 (CH, Ph), 125.7 (C-24′), 93.7 (C-1), 82.1 (C-3′), 79.0 (C-4), 78.1 (C-3), 75.4, 73.9, 72.2 (O*C*H$_2$Ph), 71.8 (C-5), 69.4 (C-6), 51.1 (C-5′), 50.8 (C-17′), 50.2 (C-13′), 44.9 (C-14′), 38.9 (C-10′), 37.4 (C-4′), 36.8 (C-23′), 35.6 (C-1′), 31.5 (C-12′), 29.1 (C-29′), 26.2, 18.1 (C-26′, C-27′), 36.9, 36.6, 31.3, 30.2, 28.7, 26.9, 25.4, 24.7, 23.0, 18.7 (C-2′, C-2, C-6′, C-7′, C-11′, C-15′, C-16′, C-20′, C-22′, C-30′), 19.7 (C-19′), 19.1 (C-21′), 16.8 (C-28′), 16.2 (C-18′) ppm. $C_{57}H_{78}O_5$ (843.23): calcd. C 81.19, H 9.32; found C 81.43, H 9.18.

(2′*R*)-/(2′*S*)-Flavanon-6-yl 3,4,6-Tri-*O*-benzyl-2-deoxy-α,β-D-*arabino*-hexopyranoside (6a,b): Reaction of **1** with 6-hydroxyflavanone (480 mg, 2 mmol) gave **6a** as a syrup {358 mg (54%) in dichloromethane [167 mg (25%) in THF at room temp.], the starting material **1** being recovered in 21% yield (88 mg) in dichloromethane [32% (133 mg) in THF at room temp. for 180 min]} or **6a**,**b** as a syrup [405 mg (62%) in THF under reflux for 180 min, α/β = 4.6/1, with 75 mg (18%) of the starting material **1** being recovered]; R_f = 0.43 (EtOAc/*n*-hexane, 1:5).

6a: IR (neat): $\tilde{\nu}$ = 1698 cm^{-1} (C=O). UV: λ_{max} (ε) = 345 nm (4341), 258 (8328). ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): δ = 7.61 (d, $^4J_{5',7'}$ = 2.0 Hz, 1 H, 5′-H), 7.45–7.18 (m, 21 H, 4 Ph, 7-′H), 6.97 (d, $^3J_{7',8'}$ = 8.8 Hz, 1 H, 8′-H), 5.67 (br. s, 1 H, 1-H), 5.43–5.37 (m, 1 H, 2′-H), 4.94, 4.91 (part A of AB system, $^2J_{AB}$ = 12.0 Hz, 1 H, OC*H*$_2$Ph), 4.76, 4.73, 4.72, 4.69 (AB system, $^2J_{AB}$ = 11.6 Hz, 2 H, OC*H*$_2$Ph), 4.63, 4.60, 4.56, 4.53 (AB system, $^2J_{AB}$ = 12.0 Hz, 2 H, OC*H*$_2$Ph), 4.47, 4.44 (part B of AB system, $^2J_{AB}$ = 12.0 Hz, 1 H, OC*H*$_2$Ph), 4.17 (td, $^3J_{3,4}$ = $^3J_{2ax,3}$ = 9.0, $^3J_{2eq,3}$ = 4.8 Hz, 1 H, 3-H), 3.87–3.60 (m, 4 H, 4-H, 5-H, 6$_A$-H, 6$_B$-H), 3.07–2.98 (m, 1 H, 3′ax-H), 2.88 (br. d, $^2J_{3'ax,3'eq}$ = 16.8 Hz, 1 H, 3′eq-H), 2.48 (dd, $^2J_{2ax,2eq}$ = 12.8, $^3J_{2eq,3}$ = 4.8 Hz, 1 H, 2eq-H), 1.95 (ddd, $^3J_{1,2ax}$ = 2.2, $^2J_{2ax,2eq}$ = 12.8, $^3J_{2ax,3}$ = 9.0 Hz, 1 H, 2ax-H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C): δ = 191.8 (C-4′, C=O), 156.9, 150.93, 150.86 (C-4′, C-6′, C-8′), 138.9, 138.8, 138.6, 138.4, 138.1 (C$_q$-Ph), 128.9, 128.5, 128.4, 127.9, 127.8, 127.7, 126.2 (C-7′, *C*H-Ph), 119.2 (C-8′), 112.9 (C-5′), 96.5 (C-1), 79.8, 79.7 (C-2′), 77.9 (C-4) 77.3 (C-3), 75.1, 73.4, 72.0 (O*C*H$_2$Ph), 71.8 (C-5), 68.6 (C-6), 44.7 or 44.6 (C-3′), 35.3 (C-2) ppm. HRMS: calcd. for $C_{42}H_{40}O_7$ 656.275482; found 656.277405.

(2′*R*)-/(2′*S*)-Flavanon-7-yl 3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranoside (7a): Reaction of **1** with 7-hydroxyflavanone (480 mg, 2 mmol) gave **7a** as a syrup (459 mg, 70%), with the starting material **1** being recovered in 14% yield (59 mg); R_f = 0.42 (EtOAc/*n*-hexane, 1:3). IR (neat): $\tilde{\nu}$ = 1689 cm^{-1} (C=O). UV: λ_{max} (ε) = 345 nm (4341), 258 (8328). ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): δ = 7.86 (d, $^3J_{5',6'}$ = 8.8 Hz, 1 H, 5′-H), 7.45–7.19 (m, 20 H, Ph), 6.75–6.70 (m, 2 H, 6′-H, 8′-H), 5.74 (br. s, 1 H, 1-H), 5.47–5.41 (m, 1 H, 2′-H), 4.92, 4.90 (part A of AB system, $^2J_{AB}$ = 10.8 Hz, 1 H, OC*H*$_2$Ph), 4.75–4.43 (m, 5 H, OC*H*$_2$Ph), 4.15 (ddd, $^3J_{2ax,3}$ = 10.8, $^3J_{2eq,3}$ = 4.8, $^3J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.82–3.48 (m, 4 H, 4-H, 5-H, 6-H), 3.02 (dd, $^3J_{2',3'ax}$ = 13.2, $^2J_{3'ax,3'eq}$ = 16.8 Hz, 1 H, 3′ax-H), 2.84 (dd, $^3J_{2',3'eq}$ = 2.4, $^2J_{3'ax,3'eq}$ = 16.8 Hz, 1 H, 3′eq-H), 2.46 (dd, $^2J_{2ax,2eq}$ = 13.2, $^3J_{2eq,3}$ = 4.8 Hz, 1 H, 2eq-H), 1.90 (ddd, $^3J_{1,2ax}$ = 2.2, $^2J_{2ax,2eq}$ = 13.2, $^3J_{2ax,3}$ = 10.8 Hz, 1 H, 2ax-H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C): δ = 190.8 (C-4, C=O), 163.3 163.0 (C-8′a, C-7′), 162.8 (C-4′a), 138.8, 138.5, 138.3, 137.9 (C$_q$, Ph), 128.5 (C-5′), 128.8, 128.4, 127.9, 127.7, 126.2, 126.1 (*C*H-Ph), 111.3, 103.9 (C-6′, C-8′) 95.9 (C-1), 79.8 (C-2′), 77.6 (C-4), 77.2 (C-3), 75.1, 73.4, 72.1 (OCH$_2$), 72.0 (C-5), 68.4 (C-6), 44.5 (C-3′), 35.1 (C-2) ppm. HRMS: calcd. for $C_{42}H_{40}O_7$ 656.275482; found 656.277406.

(2′*R*)-/(2′*S*)-Flavanon-4′-yl 3,4,6-Tri-*O*-benzyl-2-deoxy-α/β-D-*arabino*-hexopyranoside (8a,b): Reaction of **1** with 4′-hydroxyflavanone (480 mg, 2 mmol) gave **8a** as a syrup (376 mg, 57%, in dichloromethane), with the starting material **1** being recovered in 20% yield (82 mg), or **8a**,**b** as a syrup (257 mg, 39%, in THF under reflux, α/β = 8.8/1, with the starting material **1** being recovered in 8% (33 mg); R_f = 0.40 (EtOAc/*n*-hexane, 1:3).

8a: IR (neat): $\tilde{\nu}$ = 1698 cm^{-1} (C=O). UV: λ_{max} (ε) = 325.5 nm (8000), 280.0 (2246), 256.5 (8000). ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): δ = 7.94 (dd, $^3J_{5',6'}$ = 7.6, $^4J_{5',7'}$ = 1.6 Hz, 1 H, 5′-H), 7.51 (td, $^4J_{5',7'}$ = 1.6, $^3J_{7',8'}$ = $^3J_{6',7'}$ = 8.4 Hz, 1 H, 7′-H), 7.40–7.17 (m, 18 H, Ph), 7.11 (d, $^3J_{2'',3''}$ = $^3J_{5'',6''}$ = 8.0 Hz, 2 H, 3′′-H, 5′′-H), 7.08–6.98 (m, 2 H, 6′-H, 8′-H), 5.74 (d, $^3J_{1,2ax}$ = 2.4 Hz, 1 H, 1-H), 5.44 (dd, $^3J_{2',3'ax}$ = 13.6, $^3J_{2',3'eq}$ = 2.4 Hz, 1 H, 2′-H), 4.96, 4.92 (part A of AB system, $^2J_{AB}$ = 12.0 Hz, OC*H*$_2$Ph), 4.79 – 4.45 (m, 5 H, OC*H*$_2$Ph), 4.22 (td, $^3J_{2eq,3}$ = 4.8, $^3J_{2ax,3}$ = $^3J_{3,4}$ = 10.5 Hz, 1 H, 3-H), 3.88–3.76 (m, 3 H, 4-H, 5-H, 6$_A$-H), 3.62 (dd, $^2J_{6A,6B}$ = 10.5, $^3J_{5,6}$ = 5.1 Hz, 1 H, 6$_B$-H), 3.10 (dd, $^2J_{3'ax,3'eq}$ = 16.8, $^3J_{2',3'ax}$ = 13.5 Hz, 1 H, 3′ax-H), 2.89 (dd, $^3J_{2',3'eq}$ = 2.4, $^2J_{3'ax,3'eq}$ = 16.8 Hz, 1 H, 3′eq-H), 2.51 (dd, $^2J_{2ax,2eq}$ = 12.8, $^3J_{2eq,3}$ = 4.8 Hz, 1 H, 2eq-H), 1.93 (ddd, $^3J_{1,2ax}$ = 2.4, $^2J_{2ax,2eq}$ = 12.8, $^3J_{2ax,3}$ = 10.5 Hz, 1 H, 2ax-H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C): δ = 192.2 (C-4′, C=O), 161.6 (C-8′a), 156.9 (C-4′′), 138.5, 138.4, 138.0 (C$_q$, Ph), 136.2 (C-7′), 132.0 (C-1′′), 128.5, 128.4, 128.1, 127.9, 127.7 (*C*H-Ph), 127.1 (C-5′), 121.6 (C-6′), 120.9 (C-4′a), 118.1 (C-8′), 116.6 (C-3′′, C-5′′), 95.9 (C-1), 79.4 (C-2′), 75.2, 73.4, 72.0 (O*C*H$_2$), 71.3 (C-4), 68.6 (C-5), 68.5 (C-6), 44.5 (C-3′), 35.4 (C-2) ppm. HRMS: calcd. for $C_{42}H_{40}O_7$ 656.27759; found 656.277405.

Methyl (3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzylidene-α-D-glucopyranoside (9): Reaction of **1** with methyl 2-*O*-benzoyl-4,6-di-*O*-benzylidene-α-D-glucopyranoside (787 mg, 2 mmol) gave **9** as a syrup (512 mg, 64%); R_f = 0.50 (EtOAc/*n*-hexane, 1:4). $[\alpha]_D^{20}$ = +88 (*c* = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1731 cm^{-1} (C=O). UV: λ_{max} (ε) = 253 nm (1476). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 8.08 (d, *J* = 8.4 Hz, 2 H, Ph), 7.51–7.27 (m, 21 H, Ph), 7.00 (d, *J* = 8.4 Hz, 2 H, Ph), 5.63 (s, 1 H, C*H*, benzylidene), 5.56 (br. s, 1 H, 1′-H) 5.20

(dd, $^3J_{1,2}$ = 3.6, $^3J_{2,3}$ = 9.6 Hz, 1 H, 2-H), 5.05 (d, $^3J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.80, 4.76 (part A of AB system, $^2J_{AB}$ = 11.1 Hz, OCH_2Ph), 4.65–4.35 (m, 7 H, 3-H, 6eq-H, OCH_2Ph), 4.00–3.76 (m, 5 H, 4-H, 5-H, 3′-H, 5′-H, 6ax-H), 3.64–3.58 (m, 2 H, 4′-H, 6′$_A$-H), 3.48–3.43 (m, 4 H, 6′$_B$-H, OCH_3) 2.33 (dd, $^2J_{2'ax,2'eq}$ = 12.9, $^3J_{2'eq,3'}$ = 4.8 Hz, 1 H, 2′e-H), 1.70 (td, $^3J_{1',2'ax}$ = 3.0, $^2J_{2'ax,2'eq}$ = 12.9, $^3J_{2'ax,3'}$ = 12.6 Hz, 1 H, 2′ax-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 165.9 (C=O, Bz), 138.8, 138.1, 137.1 (C$_q$, Ph), 134.0, 130.7, 129.9, 129.1, 128.8, 128.7, 128.4, 128.2, 127.9, 126.8 (*C*H, Ph), 102.2 (*C*H, benzylidene), 98.8 (C-1), 98.7 (C-1′), 83.5 (C-4), 78.7 (C-4′), 77.9 (C-3′) 75.1, 74.3, 72.6 (O*C*H$_2$Ph), 72.8 (C-2), 72.5 (C-3), 71.7 (C-5′), 69.8 (C-6), 69.2 (C-6′), 62.8 (C-5), 56.2 (O*C*H$_3$), 36.3 (C-2′) ppm. $C_{48}H_{50}O_{11}$ (802.90): calcd. C 71.80, H 6.28; found C 71.93, H 6.00.

Methyl (3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-(1→4)-2,6-di-*O*-pivaloyl-α-D-*ribo*-hexopyranosid-3-ulose (10): Reaction of **1** with methyl 2,6-di-*O*-pivaloyl-α-D-*ribo*-hexopiranosid-3-ulose (720 mg, 2 mmol) gave **10** as a syrup (310 mg, 40%); R_f = 0.58 (EtOAc/toluene 1:3). $[\alpha]_D^{20}$ = +8.1 (c = 0.4, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1743 cm^{-1} (C=O). UV: λ_{max} (ε) = 245 nm (1077). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 7.35–7.17 (m, 15 H, Ph), 5.22–5.20 (m, 2 H, 1′-H, 2-H), 5.10 (d, $^3J_{1,2}$ = 4.2 Hz, 1 H, 1-H), 4.90, 4.86 (part A of AB system, $^2J_{AB}$ = 10.8 Hz, OCH_2Ph), 4.67–4.47 (m, 6 H, 6$_A$-H, OCH_2Ph), 4.36 (d, $^3J_{4,5}$ = 9.0 Hz, 1 H, 4-H) 4.25 (dd, $^3J_{5,6B}$ = 6.2, $^2J_{6A,6B}$ = 11.4 Hz, 1 H, 6$_B$-H) 4.04 (td, $^3J_{4,5}$ = $^3J_{5,6A}$ = 9.0, $^3J_{5,6B}$ = 6.2 Hz, 1 H, 5-H), 3.93 (td, $^3J_{2'ax,3'}$ = 10.2, $^3J_{2'eq,3'}$ = 6.0, $^3J_{3',4'}$ = 10.5 Hz, 1 H, 3′-H), 3.78 (dd, $^2J_{6'A,6'B}$ = 10.2, $^3J_{5',6'A}$ = 2.4 Hz, 1 H, 6′$_A$-H) 3.67–3.61 (m, 3 H, 4′-H, 5′-H, 6′$_B$-H), 3.43 (s, 3 H, OCH_3) 2.60 (dd, $^2J_{2'ax,2'eq}$ = 12.0, $^3J_{2'eq,3'}$ = 6.0 Hz, 1 H, 2′eq-H), 1.77 (ddd, $^3J_{1',2'ax}$ = 3.9, $^2J_{2'ax,2'eq}$ = 12.0, $^3J_{2'ax,3'}$ = 10.2 Hz, 1 H, 2′ax-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 197.6 (C-3), 176.5, 175.6 (C=O, Piv), 138.7, 138.1, 137.9, (C$_q$, Ph), 128.4, 128.1, 127.9, 127.6 (*C*H, Ph), 99.8 (C-1), 97.6 (C-1′), 77.7 (C-4′), 77.0 (C-3′), 75.8 (C-4), 75.1, 73.5, 71.6 (O*C*H$_2$Ph), 74.6 (C-2), 72.3 (C-5′), 70.8 (C-5), 68.4 (C-6′), 62.6 (C-6), 55.5 (O*C*H$_3$), 38.9 (Cq, Piv), 34.8 (C-2′), 27.2, 27.1 (CH$_3$, Piv) ppm. $C_{44}H_{56}O_{12}$ (776.91): calcd. C 67.94; H 7.39; found C 67.79; H 7.54.

Prop-2-en-1-yl 3,4,6-Tri-*O*-benzyl-2-deoxy-1-thio-α,β-D-*arabino*-hexopyranoside (11a,b): Reaction of **1** with prop-2-en-thiol (149 mg, 2 mmol) gave **11a**,**b** as a syrup (205 mg, 42%, α/β = 1/1); R_f = 0.55 (EtOAc/*n*-hexane, 1:7). IR (neat): $\tilde{\nu}$ = 1600 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 256 nm (890.16), 229 (568.32). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C) for **11a**: δ = 7.37–7.20 (m, 15 H, Ph), 5.87–5.76 (m, 1 H, = C*H*), 5.38 (d, $^3J_{1,2ax}$ = 5.1 Hz, 1 H, 1-H), 5.19–5.10 (m, 2 H, = CH_2), 4.92, 4.88 (part A of AB system OCH_2, $^2J_{AB}$ = 11.1 Hz, 1 H), 4.72–4.45 (m, 5 H, OCH_2Ph), 4.16 (ddd, $^3J_{4,5}$ = 9.9, $^3J_{5,6A}$ = 1.8, $^3J_{5,6B}$ = 3.6 Hz, 1 H, 5-H), 3.99–3.91 (m, 1 H, 3-H), 3.84–3.41 (m, 3 H, 4-H, 6$_A$-H, 6$_B$-H), 3.25–3.08 (m, 2 H, SCH_2), 2.32–2.24 (m, 1 H, 2eq-H), 2.07 (td, $^3J_{1,2ax}$ = 5.1, $^2J_{2ax,2eq}$ = $^3J_{2ax,3}$ = 11.7 Hz, 1 H, 2ax-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C) for **11a**: δ = 138.3 (C$_q$, Ph), 133.7 (*C*H=), 128.3, 127.9, 127.8, 127.6 (*C*H, Ph), 117.4 (=*C*H$_2$), 78.8 (C-1), 78.2 (C-3), 80.8 (C-4), 75.0, 73.4, 71.4 (O*C*H$_2$Ph), 71.1 (C-5), 69.5 (C-6), 36.4 (C-2), 33.1 (S*C*H$_2$) ppm. HRMS: calcd. for $C_{30}H_{34}O_4S$ 490.219636; found 490.217231.

1-Methylethyl 3,4,6-Tri-*O*-benzyl-2-deoxy-1-thio-α,β-D-*arabino*-hexopyranoside (12a,b): Reaction of **1** with prop-2-enthiol (153 mg, 2 mmol) gave **12a**,**b** as a syrup (320 mg, 65%, α/β = 2/1; 241 mg, 49%, α/β = 2/1, at room temp. for 24 h); R_f = 0.57 (EtOAc/*n*-hexane, 1:7). IR (neat): $\tilde{\nu}$ = 1600 cm^{-1} (C=C, Ph). UV: λ_{max} (ε) = 258.5 nm (568). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C) for **12a**: δ = 7.44–7.27 (m, 15 H, Ph), 5.61 (d, $^3J_{1,2ax}$ = 5.4 Hz, 1 H, 1-H), 5.02, 4.98 (1 H, part A of AB system, $^2J_{AB}$ = 11.1 Hz, OCH_2Ph), 4.79–4.54 (m, 5 H, OCH_2Ph), 4.29 (ddd, $^3J_{4,5}$ = 9.6, $^3J_{5,6A}$ = 1.8, $^3J_{5,6B}$ = 3.3 Hz, 1 H, 5-H), 3.90 (ddd, $^3J_{2ax,3}$ = 11.7, $^3J_{2eq,3}$ = 5.1, $^3J_{3,4}$ = 9.6 Hz, 1 H, 3-H), 3.93–3.54 (m, 3 H, 4-H, 6A-H, 6B-H), 3.30 (dq, $^3J_{CH,Me1}$ = 6.6, $^3J_{CH,Me2}$ = 6.9 Hz, 1 H, SCH), 2.48–2.34 (m, 1 H, 2eq-H), 2.15 (td, $^3J_{1,2ax}$ = 5.4, $^2J_{2ax,2eq}$ = $^3J_{2ax,3}$ = 12.6 Hz, 1-H, 2ax-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C) for **12a**: δ = 136.2, 136.0, 135.9, 135.8 (C$_q$, Ph), 125.9, 125.6, 125.4, 125.3 (CH, Ph), 77.3 (C-1), 75.8 (C-3), 78.4 (C-4), 72.6, 71.0, 69.1, (O*C*H$_2$Ph), 68.6 (C-5), 67.3 (C-6), 33.7 (C-2), 32.7 (SCH), 21.5, 21.3 (Me) ppm. $C_{30}H_{36}O_4S$ (492.67): calcd. C 73.14, H 7.37, S 6.51; found C 73.07, H 7.41, S 6.55.

1-(3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-5,6-dimethoxyindole (13): Reaction of **1** with 5,6-dimethoxyindole (355 mg, 2 mmol) gave **13** as a white solid [69 mg (12%) in dichloromethane under reflux; 117 mg (20%) in dichloromethane at room temp., 24 h; 118 mg (20%) in THF under reflux, 180 min; 115 mg (19%) in toluene under reflux], with the starting material **1** being recovered in: 77% yield (320 mg) in dichloromethane under reflux; 36% (150 mg) in dichloromethane at room temp.; 22% (92 mg) in THF; 19% (79 mg) in toluene; m.p. 101.4–102.0 °C; R_f = 0.50 (EtOAc/toluene, 1:5). $[\alpha]_D^{20}$ = +105 (c = 1, CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1648 cm^{-1} (C=C). UV: λ_{max} (ε) = 261 nm (732). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.18 (m, 16 H, Ph, 7-H), 7.01 (s, 1 H, 4-H), 6.77 (d, $^3J_{2,3}$ = 3.3 Hz, 2-H), 6.32 (d, $^3J_{2,3}$ = 3.3 Hz, 1 H, 3-H), 6.01 (br. d, $^3J_{1',2'ax}$ = 3.6 Hz, 1 H, 1′-H), 4.90–4.47 (m, 6 H, OCH_2Ph), 4.14 (ddd, $^3J_{2'ax,3'}$ = 9.6, $^3J_{2'eq,3'}$ = 4.5, $^3J_{3',4'}$ = 8.1 Hz, 1 H, H-3′), 3.91 (s, 3 H, OMe), 3.87–3.79 (m, 4 H, OMe, 4′-H), 3.71 (dd, $^3J_{5',6'A}$ = 3.6, $^2J_{6'A,6'B}$ = 10.5 Hz, 1 H, 6′$_A$-H), 3.54 (dd, $^3J_{5',6'B}$ = 2.4, $^2J_{6'A,6'B}$ = 10.5 Hz, 1 H, 6′$_B$-H), 3.32 (ddd, $^3J_{4',5'}$ = 9.6, $^3J_{5',6'A}$ = 3.6, $^3J_{5',6'B}$ = 2.4 Hz, 1 H, 5′-H), 2.72 (ddd, $^3J_{1',2'eq}$ = 1.8, $^2J_{2'eq,2'ax}$ = 14.1, $^3J_{2'eq,3'}$ = 4.5 Hz, 1 H, 2′eq-H), 2.23 (ddd, $^3J_{2'eq,3'}$ = 4.5, $^2J_{2'eq,2'ax}$ = 14.1, $^3J_{2'ax,3'}$ = 9.6 Hz, 1 H, 2′ax-H) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 146.9, 145.4 (C-5, C-6), 138.3, 138.2, 137.8 (C$_q$, Ph), 130.9, 121.6 (C-3a, C-7a), 128.6, 128.5, 128.3, 128.1, 127.9, 127.8, 127.7 (*C*H, Ph), 123.5 (C-2), 102.4 (C-3), 102.1 (C-4), 95.4 (C-7), 80.4 (C-1′), 77.6 (C-4′), 76.6 (C-3′), 74.8, 73.4, 72.4 (OCH$_2$), 71.4 (C-5′), 68.4 (C-6′), 56.2, 56.1 (OMe), 29.7 (C-2′) ppm. HRMS: calcd. for $C_{37}H_{39}NO_6$ 593.27518; found 593.27739.

Typical Experimental Procedure for the Reaction of 1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (1) with Purines Mediated by TPHB: The purine (3 mmol) was dissolved in dry THF (20 mL) and the mixture was stirred at 70 °C until total dissolution of the nucleophile. A solution of **1** (625 mg, 1.5 mmol) in dry THF (10 mL) and TPHB (80 mg, 0.24 mmol) was added to the solution of the nucleophile and the mixture was stirred at 70 °C for 180 min. After cooling to room temp. CH_2Cl_2 (30 mL) was added to the reaction mixture and the solution washed with a saturated solution of $NaHCO_3$ (20 mL). Evaporation and column chromatography with EtOAc/petroleum ether afforded the corresponding nucleoside.

9-(3,4,6-Tri-*O*-benzyl-2-deoxy-α,β-D-*arabino*-hexopyranosyl)-6-chloropurine (14a,b): Reaction of **1** with 6-chloropurine (464 mg, 3 mmol) gave **14a**,**b** as a syrup (330 mg, 39%, α/β = 2/1), with the starting material **1** being recovered in 26% yield (162 mg); R_f = 0.50 (EtOAc/petroleum ether, 1:1.5). IR (neat): $\tilde{\nu}$ = 1728, 1593, 1500, 1458, 1266 cm^{-1}. UV: λ_{max} (ε) = 266.5 nm (5782). ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C) for **14a**: δ = 8.69 (s, 1 H, 2-H), 8.30 (s, 1 H, 8-H), 7.39–7.16 (m, 15 H, Ph), 6.22 (br. t, $^3J_{1',2'ax}$ = 4.8, $^3J_{1',2'eq}$ = 4.4 Hz, 1 H, 1′-H), 4.96, 4.94 (part A of AB system, $^2J_{AB}$ = 10.8 Hz, OCH_2Ph), 4.78–4.48 (m, 5 H, OCH_2Ph), 3.98 (ddd,

$^3J_{2'ax,3'}$ = 8.7, $^3J_{2'eq,3'}$ = 4.4, $^3J_{3',4'}$ = 7.5 Hz, 1 H, 3′-H), 3.81–3.67 (m, 4 H, 4′-H, 5′-H, 6′$_A$-H, 6′$_B$-H), 3.40 (dt, $^2J_{2'eq,2'ax}$ = 14.0, $^3J_{1',2'eq}$ = $^3J_{2'eq,3'}$ = 4.4 Hz, 1 H, 2′eq-H), 2.29 (ddd, $^3J_{1',2'ax}$ = 4.8, $^2J_{2'eq,2'ax}$ = 14.0, $^3J_{2'ax,3'}$ = 8.7 Hz, 1 H, 2′ax-H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C) for **14a**: δ = 152.0 (C-2), 151.4 (C-4), 151.3 (C-6), 144.5 (C-8), 138.0, 137.8, (C$_q$, Ph), 132.1 (C-5), 128.6, 128.5, 127.9, 127.8 (CH, Ph), 80.5 (C-1′), 75.8 (C-4′), 75.5 (C-3′), 74.5 (C-5′), 74.0, 73.5, 71.6 (O*C*H$_2$), 68.3 (C-6′), 31.6 (C-2′) ppm. HRMS: calcd. for $C_{32}H_{31}{}^{35}ClN_4O_4$ 570.203383; found 570.204511.

9-(3,4,6-Tri-*O*-benzyl-2-deoxy-α,β-D-*arabino*-hexopyranosyl)-6-bromopurine (15a,b): Reaction of **1** with 6-bromopurine (600 mg, 3 mmol) gave **15a**,**b** as a white solid (414 mg, 48%, α/β = 3/1), with the starting material **1** being recovered in 23% yield (143 mg); m.p. 113.2–114.6 °C; R_f = 0.61 (EtOAc/petroleum ether, 1:1). IR (neat): $\tilde{\nu}$ = 1722, 1590, 1500, 1458, 1263 cm^{-1}. UV: λ_{max} (ε) = 240.5 nm (2376.92). ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C) for **15a**: δ = 8.57 (s, 1 H, 2-H), 8.25 (s, 1 H, 8-H), 7.28–7.09 (m, 15 H, Ph), 6.14 (br. t, $^3J_{1',2'ax}$ = 4.8, $^3J_{1',2'eq}$ = 4.4 Hz, 1 H, H-1′), 4.84, 4.81 (part A of AB system, $^2J_{AB}$ = 10.8 Hz, OC*H*$_2$Ph), 4.70–4.42 (m, 5 H, OC*H*$_2$), 3.89 (ddd, $^3J_{3',4'}$ = 7.5, $^3J_{2'ax,3'}$ = 8.8, $^3J_{2'eq,3'}$ = 4.4, 1 H, 3′-H), 3.73–3.60 (m, 4 H, 4′-H, 5′-H, 6′$_A$-H, 6′$_B$-H), 3.32 (dt, $^2J_{2'eq,2'ax}$ = 14.0, $^3J_{1',2'eq}$ = $^3J_{2'eq,3'}$ = 4.4 Hz, 1 H, 2′eq-H), 2.20 (ddd, $^3J_{1',2'ax}$ = 4.8, $^2J_{2'eq,2'ax}$ = 14.0, $^3J_{2'ax,3'}$ = 8.8 Hz, 1 H, 2′ax-H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C) for **15a**: δ = 150.8 (C-2), 149.1 (C-4), 143.4 (C-8), 142.4 (C-6), 136.9, 136.7 (Cq, Ph), 133.6 (C-5), 128.7, 128.0, 127.5, 127.4, 126.9, 126.8 (CH, Ph), 79.5 (C-1′), 74.7 (C-4′), 74.4 (C-3′), 73.5 (C-5′), 72.9, 72.5, 70.6 (O*C*H$_2$), 67.2 (C-6′), 30.6 (C-2′) ppm. $C_{32}H_{31}BrN_4O_4$ (615.52): calcd. C 62.44, H 5.08, N 9.10; found C 62.27, H 5.23, N 9.12.

Typical Experimental Procedure for the Reaction of 1 with Octanol, 6-Hydroxyflavanone and Propane-2-thiol Mediated by HY Zeolite: 1,5-Anhydro-3,4,6-tri-*O*-benzyl-2-deoxy-D-*arabino*-hex-1-enitol (**1**; 417 mg, 1 mmol) and HY zeolite (160 mg, previously activated at 140 °C) were added to a solution of the nucleophile (2.5 mmol) in dry dichloroethane (or dichloromethane) (4 mL) and the mixture was stirred under reflux for 150 min. Addition of further solvent (20 mL) was followed by filtration and evaporation of the filtrate under reduced pressure. The residue obtained was purified by column chromatography with EtOAc/*n*-hexane mixtures to afford the corresponding 2,3-unsaturated glycosides.

Octyl 4,6-Di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (16): Reaction of **1** with octanol (326 mg, 2.5 mmol) mediated by the zeolite gave **16** as a syrup [239 mg (54%) in dichloroethane; 196 mg (47%) in dichloromethane], with the starting material **1** being recovered in 2% yield (8 mg) in dichloroethane and 3% (13 mg) in dichloromethane; R_f = 0.54 (EtOAc/*n*-hexane, 1:6). $[\alpha]_D^{20}$ = +33 (*c* = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1620 cm^{-1} (C=C). UV: λ_{max} (ε) = 245.0 nm (6090). ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): δ = 7.36–7.23 (m, 10 H, Ph), 6.06 (d, $^3J_{2,3}$ = 10.0 Hz, 1 H, 3-H), 5.77 (dt, $^3J_{2,3}$ = 10.0, $^3J_{1,2}$ = $^4J_{2,4}$ = 2.0 Hz, 1 H, 2-H), 5.01 (d, $^3J_{1,2}$ = 2.0 Hz, 1 H, 1-H), 4.67–4.42 (m, 4 H, 2 OC*H*$_2$Ph), 4.17 (dd, $^4J_{2,4}$ = 2.0, $^3J_{4,5}$ = 9.2 Hz, 1H, 4-H), 3.96 (ddd, $^3J_{4,5}$ = 9.2, $^3J_{5.6A}$ = 5.4, $^3J_{5.6B}$ = 2.0 Hz, 1 H, 5-H), 3.88–3.68 (m, 3 H, 6$_A$-H, 6$_B$-H, 1′$_A$-H), 3.48 (td, $^3J_{1'A.1'B}$ = 12.8, $^3J_{1'B,2'}$ = 6.4 Hz, 1 H, 1′$_B$-H), 1.63–1.53 (m, 2 H, 2′-H), 1.27–1.25 (m, 10 H, 3′-H, 7′-H), 0.87 (t, $^3J_{7'8'}$ = 6.8 Hz, 3 H, 8′-H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C): δ = 138.3, 138.2 (C$_q$, Ph), 130.9 (C-3), 128.5, 128.4, 127.9, 127.8, 127.7 (CH, Ph) 126.8 (C-2), 94.6 (C-1), 73.3, 71.1 (O*C*H2Ph) 70.4 (C-4), 69.1 (C-5), 68.9 (C-6), 68.7 (C-1′); 31.9, 29.8, 29.4, 29.3, 26.3, 22.7 (C-2′–C-7′), 14.2 (C-8′) ppm. HRMS: calcd. for $C_{28}H_{38}O_4$ 438.278552; found 438.277010.

(2′*R*)-/(2′*S*)-Flavanon-6-yl 4,6-Di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (17): Reaction of **1** with 6-hydroxyflavanone (600 mg, 2.5 mmol) mediated by the zeolite gave **17** as a syrup [255 mg (46%) in dichloroethane; 236 mg (43%) in dichloromethane], with the starting material **1** being recovered in 7% yield (29 mg) in dichloroethane and 8% (33 mg) in dichloromethane; R_f = 0.43 (EtOAc/*n*-hexane, 1:4). IR (neat): $\tilde{\nu}$ = 1698 cm^{-1} (C=O). UV: λ_{max} (ε) = 230.0 nm (277). ^{1}H NMR (300.14 MHz, $CDCl_3$, 25 °C): δ = 7.66–7.65 (m, 1 H, 5′-H), 7.50–7.26 (m, 21 H, 4 Ph, 7′-H), 6.97 (d, $^3J_{7',8'}$ = 9.0 Hz, 1 H, 8′-H), 6.22 (d, $^3J_{2,3}$ = 10.5 Hz, 1 H, 3-H), 5.93 (ddd, $^3J_{1,2}$ = 2.7, $^4J_{2,4}$ = 2.1, $^3J_{2,3}$ = 10.5 Hz, 1 H, 2-H), 5.64 (br. s, 1 H, 1-H), 5.45–5.38 (m, 1 H, 2′-H), 4.67–4.47 (m, 4 H, OC*H*$_2$Ph), 4.23 (br. d, $^3J_{4,5}$ = 9.3, 1 H, 4-H), 4.11 (td, $^3J_{4,5}$ = 9.3, $^3J_{5,6A}$ = $^3J_{5,6B}$ = 3.0 Hz, 1 H, 5-H), 3.73–3.72 (m, 2 H, 6$_A$-H, 6$_B$-H), 3.06–2.97 (m, 1 H, 3′ax-H), 2.89–2.81 (m, $^2J_{3'ax,3'eq}$ = 16.8 Hz, 1 H, 3′eq-H) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C): δ = 192.4 (C-4′, C=O), 155.1, 149.3 (C-4′a, C-8′a), 139.5 (C$_q$, Ph), 132.6 (C-3), 129.5, 129.0, 128.5, 128.2, 126.8 (C-7′, *C*H, Ph), 126.2 (C-2), 119.8 (C-8′), 114.6 (C-5′), 94.8 (C-1), 80.4 (C-2′), 74.0, 72.0 (O*C*H$_2$), 71.1 (C-4), 70.8 (C-5), 69.4 (C-6), 45.3 (C-3′) ppm. HRMS: calcd. for $C_{35}H_{32}O_6$ 548.218761; found 548.219890.

Propan-2-yl 4,6-Di-*O*-benzyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyranoside (18): Reaction of **1** with propane-2-thiol (191 mg, 2.5 mmol) mediated by the zeolite gave **18** as a syrup [211 mg (55%) in dichloroethane; 176 mg (46%) in dichloromethane], with the starting material **1** being recovered in 2% yield (10 mg) in dichloroethane and 4% (20 mg) in dichloromethane; R_f = 0.61 (EtOAc/*n*-hexane, 1:6). $[\alpha]_D^{20}$ = –14 (*c* = 1, CH_2Cl_2). IR (neat): $\tilde{\nu}$ = 1620 cm^{-1} (C=C). UV: λ_{max} (ε) = 246.5 nm (12134). ^{1}H NMR (400.13 MHz, $CDCl_3$, 25 °C): δ = 7.22–7.11 (m, 10 H, Ph), 5.82 (d, $^3J_{2,3}$ = 9.9 Hz, 1 H, 3-H), 5.72 (ddd, $^3J_{1,2}$ = 3.0, $^4J_{2,4}$ = 1.5, $^3J_{2,3}$ = 9.9 Hz, 1 H, 2-H), 5.53 (d, $^3J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 4.58–4.28 (m, 4 H, OC*H*$_2$Ph), 4.13–4.07 (m, 2 H, 4-H, 5-H), 3.67–3.55 (m, 2 H, 6-H), 3.10–2.99 (q, $^3J_{1',2'A}$ = $^3J_{1',2'B}$ = 6.9 Hz, 1 H, 1′-H), 1.20–1.18 (m, 6 H, C*H*$_3$) ppm. ^{13}C NMR (100.62 MHz, $CDCl_3$, 25 °C): δ = 138.3, 138.2 (C$_q$, Ph), 128.1 (C-3), 128.0 (C-2), 128.5, 128.4, 128.3, 127.7, 127.8 (CH-Ph), 79.8 (C-1), 73.3, 71.1 (O*C*H$_2$Ph) 70.3 (C-4), 69.02 (C-5), 68.99 (C-6), 36.4 (S*C*H), 24.0, 23.9 (*C*H$_3$) ppm. HRMS: calcd. for $C_{23}H_{28}O_3{}^s$ 384.1745635; found 384.175915.

Acknowledgments

The authors thank the Fundação para a Ciência e Tecnologia for fellowships.

[1] P. H. Seeberger, W.-C. Haase, *Chem. Rev.* **2000**, *100*, 4349–4393.
[2] S. J. Danishefsky, M. T. Bilodeau, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1380–1419.
[3] J. Thiem, W. Klaffke, *Top. Curr. Chem.* **1990**, *154*, 285–332.
[4] V. Costantino, E. Fattorusso, C. Imperatore, A. Mangoni, *Tetrahedron* **2002**, *58*, 369–375.
[5] H. C. Lin, W. B. Yang, Y. F. Gu, C. Y. Chen, C. Y. Wu, C. H. Lin, *Org. Lett.* **2003**, *5*, 1087–1089.
[6] C. H. Marzabadi, R. W. Franck, *Tetrahedron* **2000**, *56*, 8385–8417.
[7] R. N. Farr, R. A. Outten, J. C.-Y. Cheng, G. D. Daves Jr, *Organometallics* **1990**, *9*, 3151–3156.
[8] D. Horton, W. Priebe, in *Anthracycline Antibiotics*, Academic Press, New York, **1982**, p 197.
[9] N. R. Williams, J. D. Wander, in *The Carbohydrates* (Eds.: W. Pigman, D. Horton), Academic Press, New York, **1980**; vol. IB, p. 761–798.
[10] N. R. Mallans, in *Carbohydrate Chemistry* (Ed.: J. F. Kennedy), Clarendon Press, Oxford, **1988**, p. 73.
[11] F. Arcamone, *Doxorubicin Anticancer Antibiotics*, Academic Press, New York, **1981**.

[12] T. Reichstein, E. Weiss, *Advances in Carbohydrate Chemistry* (Ed.: J. F. Kennedy), Clarendon Press: Oxford, **1988**, p 73.
[13] R. J. Ferrier, J. O. Hoberg, *Adv. Carbohydr. Chem. Biochem.* **2003**, *58*, 55–119.
[14] K. Toshima, H. Nagai, Y. Ushiki, S. Matsumara, *Synlett* **1998**, 1007–1009.
[15] E. Wieczorek, J. Thiem, *Synlett* **1998**, 467–468.
[16] S. Sabesan, S. Neira, *J. Org. Chem.* **1991**, *56*, 5468–5472.
[17] D. P. Curran, R. Ferritto, Y. Hua, *Tetrahedron Lett.* **1998**, *39*, 4937–4940.
[18] R. G. Dushin, S. J. Danishefsky, *J. Am. Chem. Soc.* **1992**, *114*, 3471–3475.
[19] V. Bolitt, C. Mioskowski, S.-G. Lee, J. R. Falck, *J. Org. Chem.* **1990**, *55*, 5812–5813.
[20] A. P. Rauter, S. Lucas, T. Almeida, D. Sacoto, V. Ribeiro, J. Justino, A. Neves, F. V. M. Silva, M. C. Oliveira, M. J. Ferreira, M.-S. Santos, E. Barbosa, *Carbohydr. Res.* **2005**, *340*, 191–201.
[21] N. Kaila, M. Blumenstein, H. Bielawska, R. W. Franck, *J. Org. Chem.* **1992**, *57*, 4576–4578.
[22] N. Kaila, H.-A. Yu, Y. Xiang, *Tetrahedron Lett.* **1995**, *36*, 5503–5506.
[23] K. C. Nicolaou, J. L. Trujillo, K. Chibale, *Tetrahedron* **1997**, *53*, 8751–8778.
[24] J. Jaunzems, D. Kashin, A. Schonberger, A. Kirschning, *Eur. J. Org. Chem.* **2004**, *16*, 3435–3446.
[25] R. J. Ferrier, *Org. React.* **2003**, *62*, 569–736.
[26] G. Descotes, J.-C. Martin, *Carbohydr. Res.* **1977**, *56*, 168–172.
[27] P. Bhate, D. Horton, W. Priebe, *Carbohydr. Res.* **1985**, *144*, 331–337.
[28] B. S. Babu, K. K. Balasuramanian, *Tetrahedron. Lett.* **2000**, *41*, 1271–1274.
[29] J. S. Yadav, B. V. S. Reddy, *Synthesis* **2002**, 511–514.
[30] M. Takhi, A. A.-H. Abbel-Rahman, R. R. Schmidt, *Tetrahedron Lett.* **2001**, *42*, 4053–4056.
[31] B. K. Bettadaiah, P. Srinivas, *Tetrahedron Lett.* **2003**, *44*, 7257–7259.
[32] J. S. Yadav, B. V. S. Reddy, L. Chandraiah, K. S. Reddy, *Carbohydr. Res.* **2001**, *332*, 221–224.
[33] B. S. Babu, K. K. Balasuramanian, *Synth. Commun.* **1999**, *29*, 4299–4305.
[34] J. S. Yadav, B. V. S. Reddy, C. V. S. R. Murthy, G. Mahesh Kumar, *Synlett* **2000**, *10*, 1450–1451.
[35] N. Raghvendra Swamy, A. Venkateswarlu, *Synthesis* **2002**, 598–600.
[36] B. Shanmugasundaram, A. K. Bose, K. K. Balasubramanian, *Tetrahedron Lett.* **2002**, *43*, 6795–6798.
[37] L. V. Dunkerton, N. K. Adair, J. M. Euske, K. T. Brady, P. D. Robinson, *J. Org. Chem.* **1988**, *53*, 845–850.
[38] E. Wieczorek, J. Thiem, *Carbohydr. Res.* **1998**, *307*, 263–270.
[39] S. Paul, N. Jayaraman, *Carbohydr. Res.* **2004**, *339*, 2197–2204.
[40] H. Kim, H. Men, C. Lee, *J. Am. Chem. Soc.* **2004**, *126*, 1336–1337.
[41] S. Xue, L. He, K.-Z. Han, X.-Q. Zheng, Q.-X. Guo, *Carbohydr. Res.* **2005**, *340*, 303–307.
[42] P. Tiwari, G. Agnihotri, A. K. Misra, *Carbohydr. Res.* **2005**, *340*, 749–752.
[43] *Zeolites for Cleaner Technologies*, in *Catalytic Science Series* (Eds.: M. Guisnet, J.-P. Gilson), Imperial College Press, London, **2002**, vol. 3.
[44] M. Guisnet, F. Ramoa-Ribeiro, *Zeólitos, um Nanomundo ao Serviço da Catálise*, Fundação Calouste Gulbenkian, Lisbon, **2004**.
[45] W. F. Hölderich, *Organic Reactions in Zeolites*, in *Comprehensive Supramolecular Chemistry* (Eds.: G. Alberti, T. Bein), Pergamon, **1996**, pp. 671–692.
[46] R. A. Sheldon, H. van Bekkum, *Fine Chemicals through Heterogeneous Catalysis*, Wiley-VCH, **2001**.
[47] R. Shukla, X. E. Verykios, R. Mutharasan, *Carbohydr. Res.* **1985**, *143*, 97 – 106.
[48] C. Moreau, R. Durand, J. Duhamet, P. Rivalier, *J. Carbohydr. Chem.* **1997**, *16*, 709–714.
[49] V. Le Strat, C. Moreau, *Catalysis Lett.* **1998**, *51*, 219–222.
[50] C. Moreau, R. Durand, F. Aliès, M. Cotillon, M.-A. Frutz, T. Théoleyre, *Ind. Crops Prod.* **2000**, *11*, 237–242.
[51] J. F. Chapat, A. Finiels, J. Joffre, C. Moreau, *J. Catal.* **1999**, *185*, 445–453.
[52] Y.-I. Matsushita, K. Sugamoto, Y. Kita, T. Matsui, *Tetrahedron Lett.* **1997**, *50*, 8709–8712.
[53] A. P. Rauter, F. Ramôa-Ribeiro, A. C. Fernandes, J. A. Figueiredo, *Tetrahedron* **1995**, *51*, 6529–6540.
[54] *Atlas of Zeolite Structures Types* available at http://www.iza-structure.org/.
[55] The empirical parameters of solvent polarity $E_T(30)$ (kcal mol^{-1}) of the solvents used in this work are the following: CH_2Cl_2 [$E_T(30)$ = 40.7], THF [$E_T(30)$ = 37.4], toluene [$E_T(30)$ = 33.9]. See: C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed., VCH, Weinheim, **1988**, pp. 20, 365–368.
[56] R. Lucas, D. Hamza, A. Lubineau, D. Bonnaffé, *Eur. J. Org. Chem.* **2004**, 2107–2117.
[57] A. Demchenko, T. Stauch, G.-J. Boons, *Synlett* **1997**, 818–820.
[58] R. J. Ferrier, *Adv. Carbohydr. Chem.* **1969**, *24*, 265–266.
[59] E. Heykants, W. H. Verrelst, R. F. Parton, P. A. Jacobs, *Stud. Surf. Sci. Catal.* **1997**, *105*, 1277–1284.
[60] I. P. Dzikh, J. M. Lopes, F. Lemos, F. Ramôa Ribeiro, *Appl. Catal. A* **1999**, *176*, 239–250.

Received: November 23, 2005
Published Online: March 16, 2006

