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Convergent and Stereoselective Synthesis of Iminosugar-Containing Gal*f* and UDP-Gal*f* Mimicks: Evaluation as Inhibitors of UDP-Gal Mutase

Virginie Liautard,[†] Valérie Desvergnes,*[,†,‡] Kenji Itoh,[§] Hung-wen Liu,[§] and Olivier R. Martin*[,†]

Institut de Chimie Organique et Analytique, Université d'Orléans, CNRS-UMR 6005, BP 6759, 45067 Orléans, France, and Division of Medicinal Chemistry, College of Pharmacy and Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, Texas 78712

olivier.martin@univ-orleans.fr; v.desvergnes@ism.u-bordeaux1.fr

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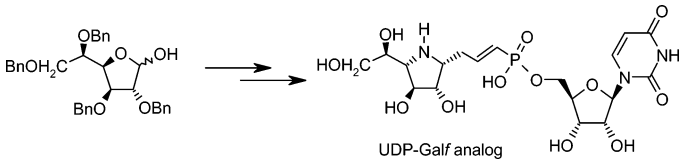

The synthesis of a UDP-Gal*f* analog incorporating a 1,4-dideoxy-1,4-imino-D-galactitol skeleton α-linked to UMP by a 3C-tether and of a series of related pyrrolidine galactofuranose mimicks is reported. These compounds were obtained by way of the highly stereoselective reaction of silylated nucleophiles with a *N*-Cbz glucofuranosylamine which afforded the corresponding open-chain product with a 1,2-*syn* stereochemistry, as predicted from pionneering studies from Kobayashi. Cyclization of these intermediates afforded α-*C*-glycosides of imino-galactofuranose carrying various functional groups in the aglycone. Further elaboration of the α-*C*-allyl substituted derivative by cross-metathesis with a uridin-5′-yl vinylphosphonate provided, after deprotection, the desired original UDP-Gal*f* mimicks. Cleavage of the benzyl ether protecting groups in the iminosugar component using BCl_3 proved critical to the success of the synthetic plan. Several of the new 1,4-dideoxy-1,4-imino-D-galactitol derivatives were evaluated as inhibitors of UGM (UDP-galactopyranose mutase) from *Escherichia coli*; however, none of them exhibited less than mM activities toward this enzyme which catalyzes a crucial step of the biosynthesis of galactofuranose-containing bacterial cell-surface glycans.

Introduction

The mycobacterial cell wall exhibits a lipidated polysaccharidic structure unique in the prokaryote reign that is essential for the microorganism growth and survival.[1] This mycolyl-arabinogalactan-peptidoglycan (mAGP) complex includes a galactan biopolymer composed of D-galactofuranose units (Gal*f*), a ring-form of galactose that occurs much less frequently than its pyranose form (Gal*p*). Members of the genus *Mycobacterium* are responsible for major health problems such as tuberculosis and leprosy. In the context of the fight against such diseases,[2] which is becoming even more critical as a result of the appearance of drug-resistant strains,[3] inhibition of the biosynthetic pathway leading to galactofuranose-containing glycans has been identified as a promising new therapeutic approach.[4] Indeed, the key intermediate of this pathway, UDP-galactofuranose (Scheme 1), is absent from mammalians;[5] it is formed from UDP-galactopyranose by a ring contraction process catalyzed by UDP-galactopyranose mutase (UPM)[6] and in the next step,

* To whom correspondence should be addressed. Tel: ++ 33 2 38 49 45 81. Fax: ++ 33 2 38 41 72 81 (O.R.M.); Tel: ++ 33 5 40 00 62 87 (V.D.).
† Université d'Orléans.
‡ Present address : Institut des Sciences Moléculaires, Université de Bordeaux 1, CNRS-UMR 5255, 351 cours de la libération, 33405 Talence, France.
§ University of Texas at Austin.

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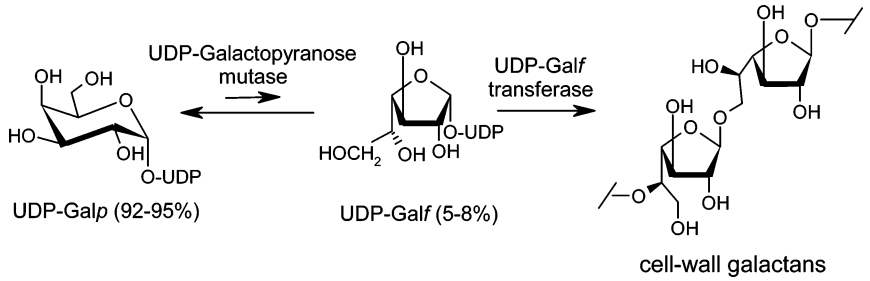
SCHEME 1. UDP-Galactofuranose and Galactan Biosynthesis



Gal*f* residues are incorporated into the galactan structure via alternating β-(1→5) and β-(1→6) linkage by a bifunctional UDP-Gal*f* transferase.[7]

Despite elegant bioorganic studies,[8] the mechanism of the unprecedented ring contraction promoted by the mutase has not yet been fully elucidated. According to most recent studies, it appears that the reaction involves a displacement mechanism in which a reduced flavin cofactor acts as a nucleophile, thus substituting UDP from UDP-Gal*p* and leading to a *N*-galactosylated intermediate which allows equilibration between the furanose and pyranose forms of galactose. As in other reactions at the anomeric carbon of glycosyl donors, these displacements are thought to occur by way of an oxocarbenium-like transition state.[9] Since iminosugars are known to be mimicks of such positively charged states, we considered that pyrrolidine-containing analogs of UDP-Gal*f* might be of interest as potential inhibitors of both the ring contraction and the glycosyl transfer reactions. In support of this proposal, pyrrolidine-based nucleoside analogs have been conceived by Schramm and Tyler[10] as inhibitors of purine nucleoside phosphorylases and related enzymes on the basis of a detailed study of transition state structures carrying a partial positive charge at the reaction site; some of these compounds turned out to be the most powerful enzyme inhibitors reported to date. More largely, iminosugars behave as inhibitors of a wide range of enzymatic processes and are under investigations as potential therapeutic agents for a diversity of diseases.[11]

In the context of our studies on iminosugars of biological interest,[12] we engaged in a research program on novel UDP-Gal*f* mimicks containing a 1,4-dideoxy-1,4-imino-D-galactitol entity. While syntheses of the parent 1,4-dideoxy-1,4-imino-D-galactitol and of a homo-derivative have been reported,[13] a single example of such *galacto*-pyrrolidine linked to uridine has been described so far.[14] We reported recently the first synthesis of a β-linked UDP-Gal*f* mimicks based on a pyrrolidinol skeleton by way of a 1,3-dipolar cycloaddition process onto a cyclic nitrone.[15] We describe in this article the full details of a synthetic study of UDP-Gal*f* mimicks in which a UMP fragment is α-linked to 1,4-dideoxy-1,4-imino-D-galactitol by a 3-carbon tether.[16] The final, fully deprotected UDP-Gal*f* analogs as well as related compounds were then tested as inhibitors of UDP-Gal mutase.

Synthetic Design. Our retrosynthetic analysis starts with D-glucose and is based on reactions of the Z-protected glucosylamine **A** as key intermediate (Scheme 2). The crucial step of the strategy is the highly stereoselective Lewis-acid-catalyzed nucleophilic addition of silylated nucleophiles onto the corresponding *N*-acyl iminium ion, a process pionneered by Kobayashi et al.[17] This process would thus lead to precursors of 'α-configured' 1,4-iminogalactitol derivatives. Then, coupling with UMP would be achieved by cross-metathesis between an α-1-*C*-allyl-1,4-imino-D-galactitol **B** and a uridin-5′-yl vinylphosphonate to provide eventually compounds of type **C**.

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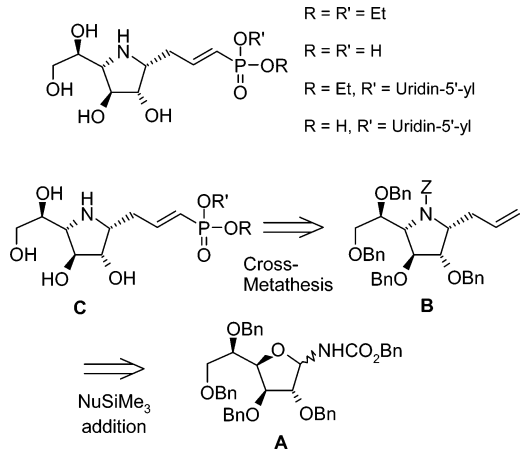
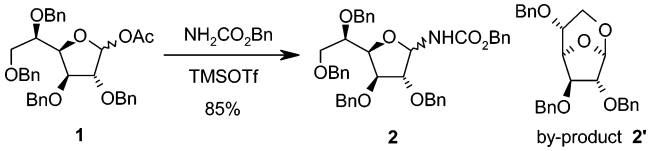
SCHEME 2. Synthetic Targets and Retrosynthesis



SCHEME 3. Synthesis of the *N*-Z Glucosylamine 2



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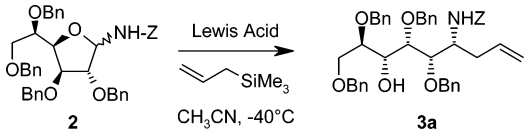

Results and Discussion

1-*O*-Acetyl-2,3,5,6-tetra-*O*-benzyl-D-glucofuranose **1** was prepared from D-glucose on a 20 g scale by a four-step procedure.[15] Under the conditions reported by Kobayashi (Z-NH_2, TMSOTf), the corresponding *N*-Z glycosylamine was obtained as a single product in 85% yield using 2 equiv of benzyl carbamate. When only 1.5 equiv or less of the carbamate was used, **2** was obtained as a mixture (from 96/4 to 84/16) with the byproduct **2′** (1,6-anhydro-2,3,5-tri-*O*-benzyl-*β*-D-glucofuranose)[18] arising from a Lewis acid-assisted regioselective de-*O*-benzylation at O-6 (Scheme 3). It is noteworthy that the reaction also works directly from 2,3,5,6-tetra-*O*-benzyl-D-glucofuranose. This reaction was recently extended to other deactivated amines (e.g., $TsNH_2$) and other sugar hemiacetals.[19]

The glucofuranosylamine **2** (α,*β* mixture) was then submitted to the Lewis acid-catalyzed reaction with allyltrimethylsilane (Scheme 4). After extensive investigations on the nature of the Lewis acid and on reaction conditions (Table 1), it was found that TMSOTf was the best reagent. 1.25 equiv of TMSOTf and 7 equiv of allyltrimethylsilane (added in portions) were necessary for the reaction to go to completion (entry 4). Compound **3a** was then isolated in a good yield of 86% and as a single *syn*-stereoisomer (see below).

Silylated Lewis acids and bismuth triflate, known to be somewhat azaphilic,[20] led to the best results. On the other hand, with the rather oxophilic BF_3 etherate, disappointing results were obtained, that could be linked to the numerous chelation sites (OBn, CO_2Bn) on the substrate, thereby decreasing the availability of the Lewis acid to form the *N*-acyl iminium ion (entry 15). Surprisingly, scandium triflate, which was expected to behave like bismuth triflate, did not lead to the conversion of the *N*-glucosylamine **2** whatever the reaction conditions used (entry 14). $HNTf_2$ is a very reactive acid but its air and moisture sensitivity limited the reproducibility of the reactions.

TABLE 1. Allylation of 2 under Various Conditions[a]

entry	lewis acid (equiv)	reaction time (h)	yield (%)
1	TMSOTf (0.1)	48	61
2	TMSOTf (0.5)	65	74
3	TMSOTf (1)	48	83
4	TMSOTf (1.25)	72	86
5	$Bi(OTf)_3$ (0.1)	48	52
6	$Bi(OTf)_3$ (0.5)	64	80
7	$Bi(OTf)_3$ (1.25)	48	81
8	TIPSOTf (0.1)	48	72
9	TIPSOTf (1)	64	80
10	TIPSOTf (1.25)	48	80
11	$HNTf_2$ (0.1)	48	36
12	$HNTf_2$ (0.5)	48	75
13	$HNTf_2$ (1.25)	48	53
14	$Sc(OTf)_3$ (1.25)	48	0
15	$BF_3.Et_2O$ (1.25)	48	8

[a] Seven equivalents of $AllSiMe_3$ were used in MeCN at −40 °C.

As a consequence, TMSOTf was used to scale up the synthesis of **3a** and to perform the addition of a variety of other silylated nucleophiles to *N*-glucofuranosylamine **2**, thus extending the synthetic value of this reaction (Scheme 5 and Table 2). Several useful functionalities could thus be introduced: with TMSCN, the reaction led to heptononitrile **3b** in an unoptimized 63% yield (entry 2). With silyl enol ethers, various keto functions were appended (entries 3, 4 and 5): a benzoylmethyl group with the silyl enol ether of acetophenone, a 2-oxocyclohexyl and a 2-oxocyclopentyl group with the silyl enol ethers of cyclohexanone and cyclopentanone respectively. It is noteworthy that a single stereoisomer was formed at the alkylation site α to the carbonyl group in cyclohexanone derivative **3d** whereas a mixture of two stereoisomers (ratio 2:1) was isolated for its cyclopentanone analog **3e**. A similar result was obtained using 2-(trimethylsiloxy)furan as the reagent: in this case, the two epimers at the alkylation site C_γ, butenolides **3f** and **3f′** (27:73), could be isolated and fully characterized. These compounds are of particular interest as synthetic precursors of disaccharide mimicks (entry 6). Despite a disappointing yield (12%) and low stereoselectivity, it was possible to obtain the protected α-amino phosphonate **3g** by reaction with diethyl trimethylsilyl phosphite (entry 7). Unsaturated aliphatic chains could also be introduced as alkyne or allene moieties in moderate yields using 3-trimethylsilyl-1,2-butadiene or propargyltrimethylsilane as reagents (entries 8 and 9). The reaction of **2** with TMS isocyanate provided in one step the original cyclic carbamate **3j** resulting from the reaction of the free 4-hydroxyl group with the isocyanate function introduced as nucleophile. This stereochemically homogeneous structure incorporates an unprecedented, stable aminal of D-glucose (entry 10).

With one exception, all addition reactions exhibited a high degree of stereoselectivity: for the reactions leading to a single new stereogenic center by formation of a C−C bond, only one product was isolated (d.e. > 98%), which was shown, after cyclization, to have a 1,2-*syn* relationship, as expected from a

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SCHEME 5. Addition of Silylated Nucleophiles to Glycosylamine 2

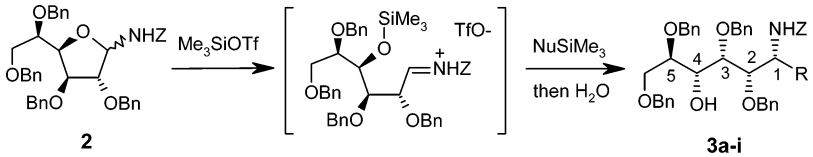
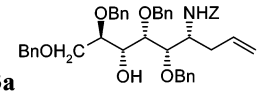
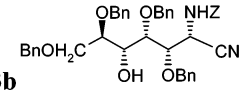
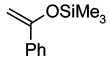
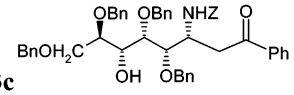
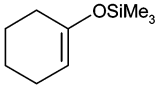
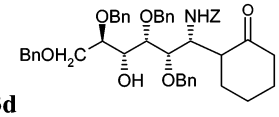
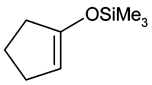
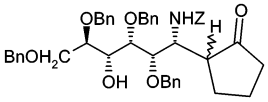
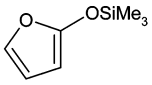
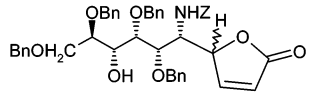
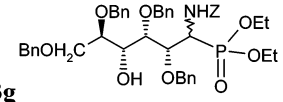
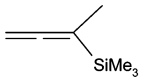
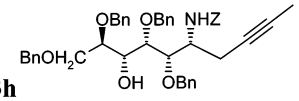
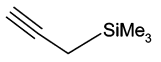
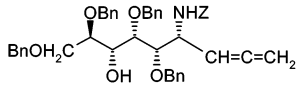
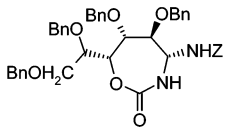


TABLE 2. Reactions of 2 with Silylated Nucleophiles $NuSiMe_3$[a]

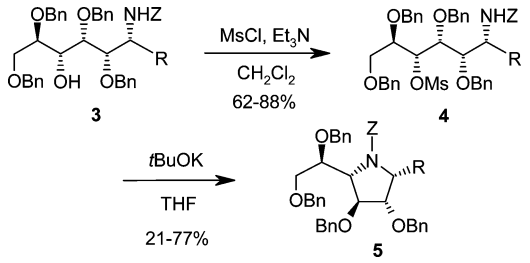
Entry	$NuSiMe_3$	Reaction time	Product	Yield (%)
1		65h	 **3a**	74
2	TMSCN	56h	 **3b**	63
3		72h	 **3c**	81
4		68h	 **3d**	68
5		48h	 **3e** (d.e. 33%)	72
6		44h	 **3f, 3f'** (d.e. 46%)	52
7	$TMSOP(OEt)_2$	71h	 **3g**	12
8		60h	 **3h**	41
9		60h	 **3i**	54
10	TMSNCO	72h	 **3j**	58

[a] All reactions were performed using 0.5 equiv of TMSOTf and 7 equiv of silylated nucleophile, in CH_3CN at −40 °C.

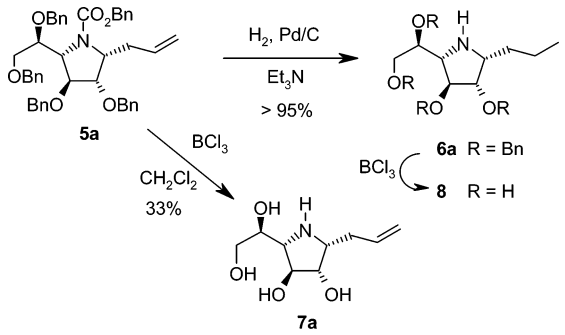
favored Re-face addition on the intermediate iminium ion.[14] The addition of the P-nucleophile, $(EtO)_2POTMS$, is the only reaction that proceeded with poor diastereoselectivity.

Next, to achieve cyclization, a classical two-step sequence involving mesylation of the free 4-OH group and subsequent treatment of the mesylate with a base (*t*-BuOK) provided the corresponding pyrrolidinol derivatives (series **5**) in modest to good yields (Scheme 6 and Table 3). In particular, the nitrile **5b** was found to be sensitive to base and we experienced some difficulties with the synthesis of this compound. Also, in most cases, better yields could be reached if the two steps from **3** were performed without isolating and purifying the mesylated

SCHEME 6. Synthesis of Pyrrolidinols 5



SCHEME 7. *N*-Deprotection of Compound 5a

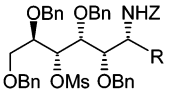
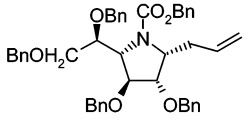
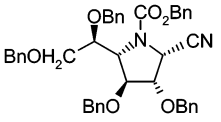
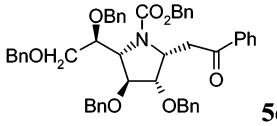
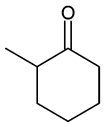
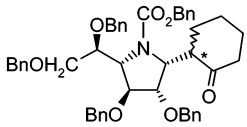
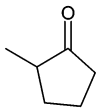
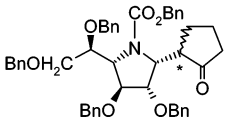
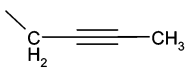
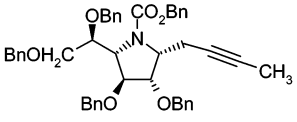
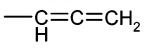
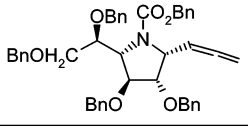


intermediate **4**. All new compounds **5a-j** are original imino-*C*-glycosyl mimicks of α-galactofuranosides. The functional groups in the aglycone can be used to tether a UDP surrogate by various synthetic approaches or to prepare analogs of other Gal*f* conjugates.

Since the carbamate rotamers in compounds of series **5** complicated their analysis by NMR, the determination of configuration of the pseudo-anomeric center was performed on the *N*-deprotected pyrrolidine **6a** (Scheme 7) and **6b**.

Vicinal coupling constants as well as clear NOESY connectivities established unambiguously the 1,2-*cis* configuration of

TABLE 3. Synthesis of Pyrrolidinols 5

Entry	 **4**	Yield of **5** (%)	Product **5**
1	**4a** R = $CH_2CH{=}CH_2$	55 (70)[a] (74)[b]	 **5a**
2	**4b** R = CN	67 (69)[b]	 **5b**
3	**4c** R = CH_2COPh	21 (40)[a]	 **5c**
4	**4d** R = 	36	 **5d**[c]
5	**4e** R = 	25	 **5e**[d]
6	**4h** R = 	63 (32)[b]	 **5h**
7	**4i** R = 	77	 **5i**

[a] Two-step sequence starting from **3**. [b] Three-step sequence starting from **2**. [c] Undetermined configuration at C*. [d] d.r. 67:33 at C*.

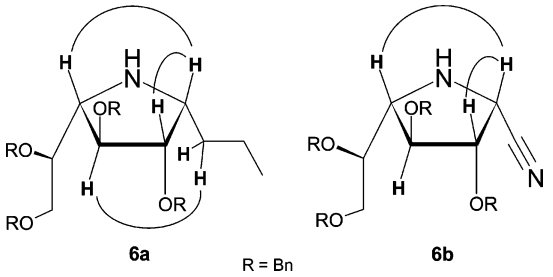


FIGURE 1. NOE correlations in compounds **6a** and **6b**.

the 1-*C*-substituted iminogalactitol derivative **6a** and **6b** and hence the 1,2-*syn* configuration of the addition product **3a** (Figure 1). By analogy and on the basis of similarities in NMR spectra of compounds in the same series, the 1,2-*cis* configuration was assigned to all pyrrolidinol derivatives **5** and the 1,2-*syn* configuration to all addition products **3**.

Further elaboration into UDP-Gal*f* mimicks was performed from the α-*C*-allylated pyrrolidinol **5a** and functionalized alkenes by cross-metathesis. This powerful coupling process is relatively insensitive to the presence of heteroatoms in the reaction partners, with the exception of amino groups.[21] It has already been used by our group[22] and others[23] to access functionalized *C*-glycosyl compounds in iminosugars carrying a deactivating protecting group at nitrogen. The coupling procedure was first investigated using diethyl vinylphosphonate (DEVP). Hoveyda-Grubbs II complex **[Ru]-3** [24] turned out to be the most efficient catalyst and provided the cross-coupling product **9** in good yield, as the (*E*)-stereoisomer only, together with some homodimerization product **10** (10%). With Nolan's catalyst **[Ru]-2**,[25] the reaction did not go to completion and, surprisingly, no conversion was observed with Grubbs II complex **[Ru]-1** (Scheme 8 and Table 4).

Moreover, the latter compound (**10**) was obtained efficiently (53% yield) via the homo-cross-coupling of **5a** using 10 mol % of **[Ru]-3** as catalyst (Scheme 8). This compound is the precursor of interesting structures mimicking fragments of galactan. The coupling products **9** and **10** were *N*- and *O*-deprotected efficiently without affecting the alkene function using a large excess of BCl_3, thus providing unsaturated phosphonate **11** and the bis-imino-*C*-disaccharide **13** as hydrochlorides in 74% and 96% yield respectively. A further treatment of **11** using $BrSiMe_3$[26] led to the free phosphonic acid **12** (as hydrobromide) and catalytic hydrogenation of **13** provided compound **14.** These new imino-*C*-glycosyl compounds are of interest as potential inhibitors of various carbohydrate-processing enzymes.

SCHEME 8. Cross-Metathesis Reactions of 5a and Deprotections

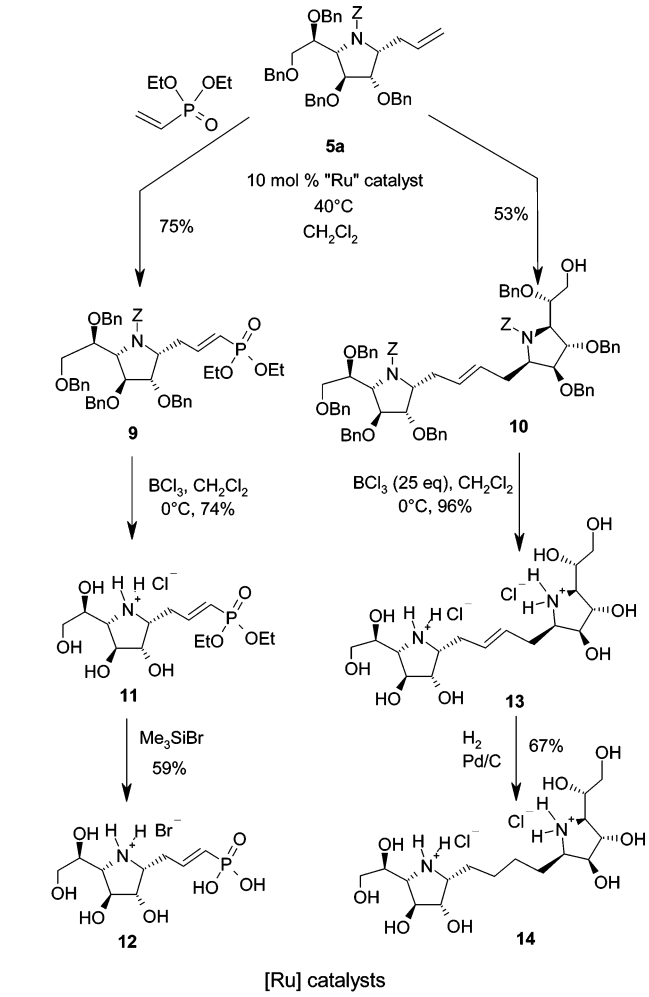


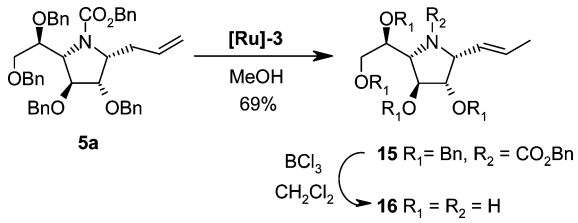
TABLE 4. Screening of Catalysts for Coupling of 5a with DEVP

[Ru] catalyst	5a	9	10
Grubbs II **[Ru]−1**	100%	−	−
Nolan **[Ru]−2**	9%	68%	8%
Hoveyda-Grubbs II **[Ru]−3**	−	75%	10%

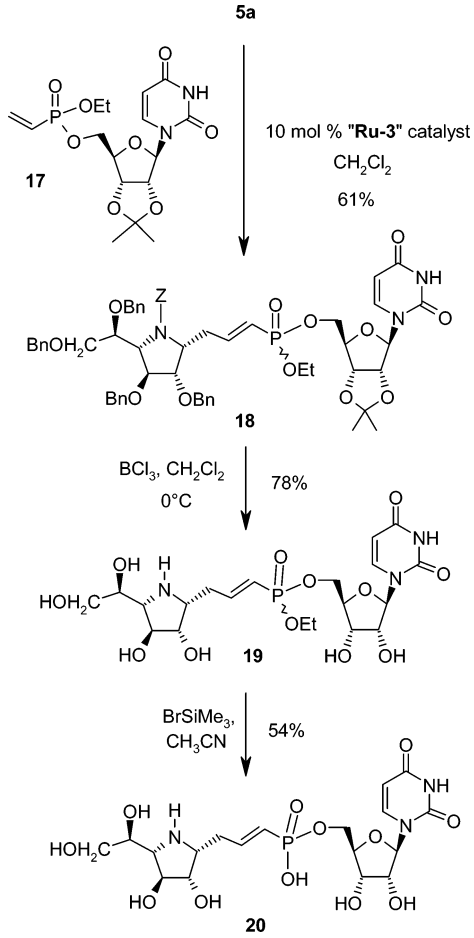
Interestingly, the allyl group of **5a** could be isomerized into a 1-propenyl substituent to give compound **15** (69%) in the presence of Hoveyda's catalyst when the reaction was performed in methanol at higher temperature, as shown recently by Hanessian and co-workers.[27] The same isomerization process was also successful (in 61% yield) using $Pd(MeCN)_2Cl_2$ (10 mol % in toluene at 60 °C for 48 h).[28] Cross-metathesis with

(21) Compain, P. *Adv. Synth. Catal.* **2007**, *349*, 1829−1846.
(22) Godin, G.; Compain, P.; Martin, O. R. *Org. Lett.* **2003**, *5*, 3269−3272.
(23) Dondoni, A.; Giovannini, P. P.; Perrone, D. *J. Org. Chem.* **2005**, *70*, 5508−5518.
(24) Kingsbury, J. S.; Harrity, J. P. A.; Bonitatebus, P. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 791−799. See also: Vehlow, K.; Maechling, S.; Blechert, S. *Organometallics* **2006**, *25*, 25−28.
(25) (a) Huang, J.; Stevens, E. D.; Nolan, S. P.; Petersen, J. L. *J. Am. Chem. Soc.* **1999**, *121*, 2674−2678. (b) Amblard, F.; Nolan, S. P.; Schinazi, R. F.; Agrofoglio, L. A. *Tetrahedron* **2005**, *61*, 537−544. For an application to a homodimerization process, see, e.g., Grellepois, F.; Crousse, B.; Bonnet-Delpon, D.; Bégué, J. P. *Org. Lett.* **2005**, *7*, 5219−5222.
(26) For phosphonate deprotection using $BrSiMe_3$, see, e.g.: (a) Vidil, C.; Morère, A.; Garcia, M.; Barragan, V.; Hamdaoui, B.; Rochefort, H.; Montero, J.-L. *Eur. J. Org. Chem.* **1999**, 447−450. (b) Ladame, S.; Fauré, R.; Denier, C.; Lakhdar-Ghazal, F.; Wilson, M. *Org. Biomol. Chem.* **2005**, *3*, 2070−2072.
(27) Hanessian, S.; Giroux, S.; Larsson, A. *Org. Lett.* **2006**, *24*, 5482−5484.
(28) Chang, G. X.; Lowary, T. *Tetrahedron Lett.* **2006**, *47*, 4561−4564.

SCHEME 9. Isomerization of Allyl Group in 5a



SCHEME 10. Synthesis of UDP-Gal*f* Mimick 20



other alkenes however was unsuccessful from **15**. Deprotection of **15** by the action of excess BCl_3 provided **16** (Scheme 9).

The same coupling approach was used to obtain the α-linked UDP-Gal*f* mimicks **20** using the ethyl uridin-5′-yl vinylphosphonate **17**[15] as cross-metathesis partner (Scheme 10). As with the previous reagent, total conversion of compound **5a** was achieved using Hoveyda-Grubbs II complex **[Ru]-3** as the catalyst. The iminosugar-nucleotide conjugate **18** was thus obtained as a mixture of non-separable *P**-epimers in 61% yield together with a small amount of compound **10** (13%). A two-step deprotection sequence led to the fully deprotected target compound **20** (42% overall). Treatment of **18** with BCl_3 in excess at 0 °C promoted the complete deprotection of the ribofuranose and iminogalactitol moieties and led to the phosphonic diester **19**. The ethyl phosphonate could then be cleaved selectively by reacting **19** with $BrSiMe_3$ to provide UDP-Gal*f* analog **20**. This compound incorporates an iminosugar moiety that mimicks the putative galactofuranosyl cation involved in the reactions catalyzed by UDP-Gal mutase and/or UDP-Gal*f* transferases and the three-carbon linker places the nucleotide fragment at an appropriate distance with respect to the pseudosugar moiety. To the best of our knowledge this compound is the closest iminosugar-based analog of UDP-Gal*f* ever reported.

TABLE 5. Inhibition of *E. Coli* UGM by Selected Compounds[a]

compound #	inhibitor concentration	residual activity
7a	25 mM	61%
8	2.5 mM	52.1%
13	2.5 mM	50%
14	2.5 mM	36.9%
16	2.5 mM	59.2%
19	25 mM	52%
20	2.5 mM	43%

[a] See experimental procedures in ref 15b.

The inhibitory activity of compounds **7a**, **8**, **13**, **14**, **16**, **19**, and **20** toward UGM from *Escherichia coli* was then evaluated and the results are reported in Table 5. Inhibition assays on the purified enzyme were conducted in the reverse direction in which UDP-Gal*f* is converted to UDP-Gal*p* using an HPLC method developped by Lee and co-workers[29] under the same conditions as previously reported.[15b] Residual activity is expressed in % of the activity in absence of inhibitor.

All derivatives tested were found to exhibit weak inhibition of UGM. Residual activity is in the order of 50% for most compounds at 2.5 mM inhibitor concentration. Noticably, the presence of the UMP motif, which was anticipated to provide significant binding, increased only to a very minor extent the activity of the compounds carrying a simple 3-carbon substituent at C-1. This is even more surprising in view of Kiessling's recent work on chemical probes for UGM which suggested that the presence of an aromatic group mimicking uracil is essential for better binding with the enzyme.[30] Most of the recognition by the enzyme appears to arise from the 1,4-iminogalactitol moiety, and dimerization of this unit, as in **13** and **14**, contributes to enhance the inhibitory activity. Compound **14** is indeed the most active inhibitor of the series.

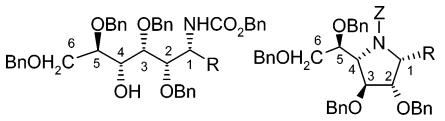
In conclusion, we report in this article a convenient and highly stereoselective methodology for the synthesis of a diversity of α-1-*C*-substituted-1,4-dideoxy-1,4-imino-D-galactitols; such compounds constitute novel, original galactofuranoside mimicks. One of these compounds was converted into UDP-Gal*f* analogs (**19**, **20**) in which UMP is linked to the *galacto*-pyrrolidinol by a 3-C tether, thereby mimicking closely the structure of the natural sugar nucleotide; carbon-linked disaccharide analogs (**13**, **14**) were also generated from the same precursor. Whereas the activity of compounds such as **19** and **20** as inhibitors of UGM was found to be weak, these sugar nucleotide analogs remain promising chemical probes of the Gal*f* transfer process involved in the biosynthesis of mycobacterial galactans. In addition the 1-*C*-substituted iminogalactitol derivatives and the corresponding dimers are of interest as potential inhibitors of various glycofuranosidases. Further biological investigations on these compounds are in progress and the results will be reported in due course.

(29) Lee, R.; Monsey, D.; Weston, A.; Duncan, K.; Rithner, C.; McNeil, M. *Anal. Biochem.* **1996**, *242*, 1−7.

(30) Carlsson, E. E.; May, J. F.; Kiessling, L. L. *Chem. Biol.* **2006**, *13*, 825−837.

Experimental Section

General Procedure A: Addition of Silylated Nucleophiles. In a dry 10 mL flask, under Ar, the silylated nucleophile ($NuSiMe_3$ in Table 2) (1.45 mmol, 7 equiv) was added to a solution of *N*-benzyloxycarbonyl-2,3,5,6-tetra-*O*-benzyl-α,*β*-D-glucofuranosylamine **2** (140 mg, 0.21 mmol)[19] in anhydrous acetonitrile (2.1 mL). The mixture was stirred at −40 °C during 15 min and trimethylsilyl triflate (19 μL, 0.10 mmol, 0.5 equiv) was then added by portions to the colorless solution. The mixture was stirred at −40 °C during 20−82 h, and the reaction was then quenched with saturated aqueous $NaHCO_3$ (1 mL). Ethyl acetate (20 mL) was added and the organic layer was separated, washed with brine (20 mL) and dried over sodium sulfate. The solvents were removed by evaporation under vacuum to afford a brown oil which was purified by flash chromatography (toluene/acetone 99:1 to 98:2 containing a trace of Et_3N unless otherwise indicated).



3 **5**

1(*R*)-1-*C*-Allyl-2,3,5,6-tetra-*O*-benzyl-1-benzyloxycarbonylamino-1-deoxy-D-glucitol (3a). According to general procedure **A,** compound **3a** was obtained as a colorless oil (129 mg, 86%) from **2** (140 mg, 0.21 mmol) after a stirring time of 72 h. $[\alpha]^{25}_D$ −6 (c = 1.22, $CHCl_3$); IR (NaCl, cm^{-1}) 3436, 3029, 3013, 2927, 2866, 1716, 1498, 1454, 1333, 1216, 1097, 1060, 1027; ^1H NMR (500 MHz, $CDCl_3$) δ 2.18−2.31 (m, 2H, $CH_2CH{=}CH_2$), 2.56 (d, 1H, $J \approx 9$ Hz, OH), 3.55−3.59 (m, 1H, H4), 3.62−3.68 (m, 2H, H5, H6a), 3.72 (d, 1H, $J \approx 8$ Hz, H2), 3.81−3.91 (m, 3H, H1, H3, H6b), 4.22 (d, 1H, $J \approx 11$ Hz, OCH_2Ph), 4.29 (d, 1H, $J \approx 11.5$ Hz, OCH_2Ph), 4.43−4.49 (m, 3H, OCH_2Ph), 4.63 (d, 2H, $J \approx 11.5$ Hz, OCH_2Ph), 4.73 (d, 1H, $J \approx 11$ Hz, OCH_2Ph), 4.86−4.96 (m, 3H, OCH_2Ph, $CH_2{=}CH$), 5.04 (d, 1H, $J \approx 12.5$ Hz, OCH_2Ph) 5.13 (d, 1H, $J \approx 9.5$ Hz, NH), 5.62−5.70 (m, 1H, $CH{=}CH_2$), 7.08−7.26 (m, 25H, $CH_{Ar's}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.3 (CH_2-$CH{=}CH_2$), 51.5 (*C*1), 66.8 (OCH_2Ph), 70.9 (*C*5), 71.2 (*C*6), 71.7, 73.7, 74.7, and 75.2 (OCH_2Ph), 78.2 (*C*3+*C*4), 79.7 (*C*2), 117.9 ($CH_2{=}CH$), 127.5−128.6 ($CH_{Ar's}$), 134.7 ($CH{=}CH_2$), 136.7, 138.3, 138.4, and 138.6 (Cq_{Ar}), 156.1 (*C*=O); (+) MS (ESI): m/z = 733.5 $[M + NH_4]^+$, 738.5 $[M + Na]^+$; HRMS (ESI): calcd for $C_{45}H_{49}NNaO_7$: m/z = 738.3407 $[M + Na]^+$, found : m/z = 738.3401. Anal. Calcd. for $C_{45}H_{49}NO_7$: C, 75.50; H, 6.90; N, 1.96. Found: C, 75.72; H, 6.96; N, 1.84.

3,4,6,7-Tetra-*O*-benzyl-2-benzyloxycarbonylamino-2-deoxy-D-*glycero*-D-*ido*-heptono-nitrile (3b). According to general procedure **A**, compound **3b** was obtained as a colorless oil (35.1 mg, 63%) from **2** (53.4 mg, 0.079 mmol) using 0.5 equiv of trimethylsilyl triflate and after a stirring time of 56 h. $[\alpha]^{25}_D$ −4 (c = 0.45, $CHCl_3$); IR (NaCl, cm^{-1}) 3427, 3033, 2253, 1726, 1497, 1455, 1271, 1215, 1096, 1028; ^1H NMR (500 MHz, $CDCl_3$) δ 2.70 (broad s, 1H, OH), 3.57−3.61 (m, 1H, H4), 3.65−3.73 (m, 1H, H6a), 3.78−3.82 (m, 2H, H6b + H5), 3.85 (d, 1H, $J \approx 7$ Hz, H3), 4.03−4.05 (m, 1H, H2), 4.28 (t, 2H, $J \approx 10.5$ Hz, OCH_2Ph), 4.50−4.65 (m, 4H, OCH_2Ph), 4.71 (AB, 2H, $J \approx 11$ Hz, OCH_2Ph), 4.91−4.93 (m, 1H, H-1), 5.02−5.12 (m, 2H, OCH_2Ph), 5.67−5.69 (m, 1H, N*H*), 7.14−7.32 (m, 25H, $CH_{Ar's}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 43.8 (*C*1), 67.9 (OCH_2Ph), 70.2 (*C*6, *C*5), 71.8, 73.7, 74.5, and 75.0 (OCH_2Ph), 76.6 (*C*3), 77.6 (*C*4), 78.0 (*C*2), 118.2 (*C*N), 127.8−130.0 ($CH_{Ar's}$), 135.8, 136.8, 137.7, 138.0, and 138.3 (Cq_{Ar}), 155.4 (*C*=O); (+) MS (ESI) : m/z = 719 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{43}H_{44}N_2NaO_7$: m/z = 723.3046 $[M + Na]^+$, found: m/z = 723.3041.

4,5,7,8-Tetra-*O*-benzyl-3-benzyloxycarbonylamino-2,3-dideoxy-1-*C*-phenyl-D-*glycero*-D-*ido*-1-octulose (3c). According to general procedure **A**, compound **3c** was obtained as a colorless oil (200 mg, 81%) from **2** (208 mg, 0.31 mmol), using 0.5 equiv of trimethylsilyl triflate and after a stirring time of 72 h. $[\alpha]^{25}_D$ −3 (c = 0.69, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 2.93 (d, 1H, $J \approx 7.5$ Hz, OH), 3.01−3.05 (m, 1H, CH_2COPh), 3.19−3.26 (m, 1H, CH_2COPh), 3.73−3.79 (m, 2H, H2 + H6a), 3.92−3.95 (m, 4H, H6b + H5 + H3 + H4), 4.33−4.49 (m, 5H, H1 + OCH_2Ph), 4.55 (broad s, 2H, OCH_2Ph), 4.70−4.77 (m, 2H, OCH_2Ph), 5.02 (d, 1H, $J \approx 12$ Hz, OCH_2Ph), 5.07 (d, 1H, $J \approx 12$ Hz, OCH_2Ph), 5.43−5.47 (m, 1H, NH), 7.08−7.81 (m, 30H, $H_{Ar's}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.5 (CH_2COPh), 48.3 (C1), 66.9 (OCH_2Ph), 70.3 (C5), 71.2 (C6), 71.7, 73.6, 74.4, and 75.0 (OCH_2Ph), 77.9 (C3 or C4), 78.3 (*C*2), 78.7 (C4 or C3), 127.5−128.6, 133.3, 136.5, 138.0, 138.3, 138.4, and 138.8 (Cq_{Ar}), 155.9 (*C*=O), 198.4 (*C*=O); HRMS (ESI) calcd for $C_{50}H_{51}NNaO_8$: m/z = 816.3512 $[M + Na]^+$; found: m/z = 816.3506.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-1-benzyloxycarbonylamino-1-deoxy-1-*C*-(2-oxocyclohexyl)-D-glucitol (3d). According to general procedure **A**, compound **3d** (107 mg, 68%) was obtained from compound **2** (138.1 mg, 0.205 mmol) as a single product and as a colorless oil after purification by flash chromatography (EP/AcOEt 4:1). $[\alpha]^{25}_D$ −19 (c = 0.99, $CHCl_3$); IR (NaCl, cm^{-1}) 3435, 3063, 3031, 2935, 2863, 1718, 1702, 1498, 1454, 1210, 1072, 1028; ^1H NMR (250 MHz, $CDCl_3$) δ 1.48−2.10 (m, 7H), 2.17−2.33 (m, 1H), 2.78−3.00 (m, 2H, OH and C*H*CO), 3.57−3.75 (m, 2H, H5 + H6a), 3.77−3.90 (m, 2H, H3 + H6b), 3.92−4.06 (m, 2H, H2 + H4), 4.08−4.18 (m, 1H, H1), 4.24 (d, 1H, $J \approx 11$ Hz, OCH_2Ph), 4.31 (d, 1H, $J \approx 11.5$ Hz, OCH_2Ph), 4.43−4.59 (m, 4H, OCH_2-Ph), 4.60−4.72 (m, 2H, OCH_2Ph), 5.52 (d, 1H, $J \approx 10$ Hz, NH), 7.06−7.40 (m, 25H, $CH_{Ar's}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.4, 27.8, 31.3, 42.4, and 52.1 (cyclohexyl *C*H2 and *C*H), 53.5 (*C*1), 66.8 (OCH_2Ph), 70.0 (*C*4), 71.0 (*C*6), 71.9, 73.6, 73.7, and 74.0 (OCH_2Ph), 77.0 (*C*3), 77.3 (*C*2), 78.6 (*C*5), 127.5−128.8 ($CH_{Ar's}$), 136.8, 138.0, 138.2, 138.3, and 138.7 (Cq_{Ar}), 156.8 (C=O), 211.7 (C=O); (+) MS (ESI) : m/z = 789.5 $[M + NH_4]^+$, 795.0 $[M + Na]^+$; HRMS (ESI) calcd for $C_{48}H_{53}NNaO_8$: m/z = 794.3669 $[M + Na]^+$; found : m/z = 794.3672.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-1-benzyloxycarbonylamino-1-deoxy-1-*C*-(2-oxocyclopentyl)-D-glucitol (3e). According to general procedure **A**, compound **3e** (367.5 mg, 70%) was obtained from compound **2** (463 mg, 0.688 mmol) as a colorless oil (mixture of diastereoisomers at cp-*C*2) after purification by flash chromatography (EP/ AcOEt 5:2 to 2:1). IR (NaCl, cm^{-1}) 3435, 3063, 3017, 1720, 1454, 1404, 1217, 1093, 1028; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22−2.42 (m, 7H), 2.71 (br s, 1H, OH), 3.59−4.05 (m, 6H), 4.20−4.95 (m, 8H, OCH_2Ph and H2), 5.00−5.42 (m, 2H, OCH_2-Ph and NH), 7.11−7.42 (m, 25H, $CH_{Ar's}$); ^{13}C NMR (100 MHz, $CDCl_3$; d1 and d2 for diast. 1 and 2, respectively; cp for cyclopentyl) δ 20.3 (d1, cp-*C*4), 20.5 (d2, cp-*C*4), 27.3 (d1, cp-*C*3), 27.7 (d2, cp-*C*3), 38.7 (d1, cp-*C*5), 38.9 (d2, cp-*C*5), 50.2 (d2, cp-*C*2), 50.9 (d1, cp-*C*2), 51.2 (d1, *C*1), 52.3 (d2, *C*1), 67.0 (OCH_2Ph), 70.3 (d1, *C*4), 70.7 (d2, *C*4), 71.0 (d2, *C*6), 71.5 (d1, *C*6), 71.7, 71.8, 73.58, 73.63, 74.2, 74.38, 74.44, and 74.8 (OCH_2Ph), 77.4 (*C*3), 77.5 (*C*3), 77.9 (d1, *C*5), 78.1 (d2, *C*5), 78.3 (d1, *C*2), 78.5 (d2, *C*2), 127.4−128.5 ($CH_{Ar's}$), 136.6, 136.7, 137.9, 138.2, 138.3, 138.38, 138.40, 138.5, 138.6, and 138.9 (Cq_{Ar}), 156.3 (*C*=O), 156.7 (*C*=O), 218.9 (cp-*C*1), 219.2 (cp-*C*1); (+) MS (ESI) : m/z = 775.5 $[M + NH_4]^+$, 780.0 $[M + Na]^+$; HRMS (ESI) calcd for $C_{47}H_{51}NNaO_8$: m/z = 780.3512 $[M + Na]^+$; found : m/z = 780.3513.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-1-benzyloxycarbonylamino-1-*C*-but-2-ynyl-1-deoxy-D-glucitol (3h). According to general procedure **A**, compound **3h** (100 mg, 47%) was obtained from compound **2** (196 mg, 0.291 mmol) as a colorless oil after purification by flash chromatography (Toluene/ AcOEt 16:1). $[\alpha]^{25}_D$ −6 (c = 0.71, $CHCl_3$); IR (NaCl, cm^{-1}) 3429, 3063, 3032, 2919, 2866, 1718, 1498, 1454, 1334, 1266, 1216, 1095, 1062, 1027; ^1H NMR (400 MHz, $CDCl_3$) δ 1.71 (s, 3H, CH_3), 2.30−2.57 (m, 2H, CH_2), 2.66 (br s, 1H, OH), 3.56−3.71 (m, 1H, H5), 3.73−3.82 (m, 1H, H4), 3.85−3.94 (m, 3H, 2H6 and H3), 3.98−4.07 (m, 1H, H1), 4.09−4.18 (m, 1H, H2), 4.23−4.42 (m, 2H, OCH_2Ph), 4.49−5.00 (m,

7H, OCH_2Ph), 5.07−5.17 (m, 1H, OCH_2Ph), 5.24 (d, 1H, $J \approx 9.6$ Hz, NH), 7.18−7.43 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.6 (CH_3), 23.6 (CH_2), 51.2 (*C*1), 66.9 (O*C*H_2Ph), 70.5 (*C*4), 71.2 (C6), 71.7, 73.6, and 74.5 (O*C*H_2Ph), 75.36 (C_{alkyne}-CH_3), 75.41 (O*C*H_2Ph), 76.8 (C_{alkyne}-CH_2), 77.9 (*C*3), 78.2 (*C*5), 78.9 (*C*2), 127.5−128.6 (*C*$H_{Ar's}$), 136.6, 138.2, 138.3, and 138.7 (Cq_{Ar}), 155.9 (*C*═O); (+) MS (ESI) : m/z = 728 $[M + H]^+$, 745.5 $[M + NH_4]^+$, 750.5 $[M + Na]^+$; HRMS (ESI) calcd for $C_{46}H_{49}NNaO_7$: m/z = 750.3407 $[M + Na]^+$, found : m/z = 750.3416.

1(*R*)-1-*C*-Allenyl-2,3,5,6-tetra-*O*-benzyl-1-benzyloxycarbonylamino-1-deoxy-D-glucitol (3i). According to general procedure **A**, compound **3i** (149 mg, 54%) was obtained from compound **2** (259 mg, 0.233 mmol) as a colorless oil after purification by flash chromatography (PE/ AcOEt 7:1 to 6:1). $[\alpha]^{25}_D$ −1.6 (c = 3.14, $CHCl_3$); IR (NaCl, cm^{-1}) 3432, 3063, 3031, 2926, 2867, 1958, 1719, 1498, 1455, 1399, 1337, 1276, 1215, 1096, 1062, 1028, 854; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67 (d, 1H, $J \approx 8.8$ Hz, OH), 3.57−3.97 (m, 6H), 4.31 (d, 1H, $J \approx 11.2$ Hz, OCH_2Ph), 4.35 (d, 1H, $J \approx 11.8$ Hz, OCH_2Ph), 4.47−4.65 (m, 4H, OCH_2Ph and H1), 4.67−4.84 (m, 5H, OCH_2Ph and CH_2═), 4.98 (d, 1H, $J \approx 12$ Hz, OCH_2-Ph), 5.14 (d, 1H, $J \approx 12$ Hz, OCH_2Ph), 5.24 (q, 1H, $J \approx 5.9$ Hz, CH═), 5.38 (d, 1H, $J \approx 9.2$ Hz, NH), 7.17−7.38 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.4 (*C*1), 66.9 (O*C*H_2Ph), 70.9 (*C*6), 71.7, 73.6, 74.8, and 75.4 (O*C*H_2Ph), 78.0 (*C*H), 78.6 (*C*H_2═), 81.5 (*C*H), 91.8 (*C*H═), 127.5−128.6 (*C*$H_{Ar's}$), 136.6, 138.19, 138.21, 138.4, and 138.6 (Cq_{Ar}), 156.1 (C═O), 207.6 (═C═); (+) MS (ESI) : m/z = 714.5 $[M + H]^+$, 731.5 $[M + NH_4]^+$, 736.5 $[M + Na]^+$; HRMS (ESI) calcd for $C_{45}H_{47}NNaO_7$: m/z = 736.3250 $[M + Na]^+$; found : m/z = 736.3260.

2,3,5,6-Tetra-*O*-benzyl-D-glucose aminal N_S-benzyl carbamate N_R,*O*-cyclic carbamate (3j). According to general procedure **A**, compound **3j** (96.5 mg, 58%) was obtained from compound **2** (157 mg, 0.233 mmol) as a colorless oil after purification by flash chromatography (PE/AcOEt 3:1). $[\alpha]^{25}_D$ −26 (c =1.05, $CHCl_3$); IR (NaCl, cm^{-1}) 3392, 3321, 3063, 3032, 2869, 1732, 1513, 1499, 1455, 1266, 1309, 1227, 1102, 1028, 1046; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (t, 1H, $J \approx 3.6$ Hz, H2), 3.80 (dd, 1H, $J \approx 4.4$ and 10.4 Hz, H6a), 3.88 (ddd, 1H, $J \approx 1.6$, 4.4 and 9.6 Hz, H5), 3.99 (dd, 1H, $J \approx 1.6$ and 10.4 Hz, H6b), 4.09 (d, 1H, $J \approx 3.6$ Hz, H3), 4.25−4.39 (m, 3H, OCH_2Ph), 4.45−4.65 (m, 5H, OCH_2Ph and H4), 4.79 (d, 1H, $J \approx 11.6$ Hz, OCH_2Ph), 4.95−5.01 (m, 2H, OCH_2Ph and H1), 5.12 (d, 1H, $J \approx 12.4$ Hz, OCH_2Ph), 5.86 (d, 1H, $J \approx 6$ Hz, NH), 6.99 (d, 1H, $J \approx 9.2$ Hz, NH), 7.04−7.36 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 61.0 (*C*1), 67.2 (O*C*H_2-Ph), 69.1 (*C*6), 71.0 (*C*2), 71.8, 72.0, 73.3, and 73.6 (O*C*H_2Ph), 74.9 (*C*4), 75.6 (*C*5), 76.0 (*C*3), 127.6−128.7 (*C*$H_{Ar's}$), 136.1, 136.7, 137.0, 138.3, and 138.4 (Cq_{Ar}), 155.5 (C═O), 157.3 (C═O); (+) MS (ESI) : m/z = 717.5 $[M + H]^+$, 734.5 $[M + NH_4]^+$, 739.5 $[M + Na]^+$; HRMS (ESI) calcd for $C_{43}H_{44}N_2NaO_8$: m/z = 739.2995 $[M + Na]^+$; found : m/z = 739.2980.

General Procedure B: Cyclization Procedure. In a dry flask (10 mL), under Ar, methanesulfonyl chloride (8.2 μL, 0.11 mmol, 2.1 equiv) was added by portions to a solution of substrate **3** (38 mg, 0.053 mmol) in anhydrous dichloromethane (530 μL) containing triethylamine (16 μL, 0.12 mmol, 2.2 equiv). The yellow mixture was stirred at room temperature for 5−12 h. After total conversion (TLC monitoring), the reaction was quenched with saturated aqueous NH_4Cl (1 mL). Ethyl acetate (20 mL) was added, the organic layer was separated, washed with brine (20 mL) and dried over sodium sulfate. The solvents were then evaporated, thus providing the corresponding methanesulfonate **4** as a yellow oil which could be used in the next step without further purification.

Crude **4** (142 mg, 0.18 mmol) was dissolved in anhydrous THF (1.8 mL) and *t*-BuOK (20.12 mg, 0.18 mmol) was added. The mixture was stirred during 12−24 h at room temperature. After total conversion (TLC monitoring), the reaction was quenched with saturated aqueous NH_4Cl (1 mL). Ethyl acetate (20 mL) was added, the organic layer was separated, washed with brine (20 mL) and dried over sodium sulfate. Then the solvents were evaporated, thus providing a colorless oil which was purified by flash chromatography (PE/AcOEt 7:1 containing a trace of Et_3N).

1(*R*)-1-*C*-Allyl-2,3,5,6-tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1,4-dideoxy-1,4-imino-D-galactitol (5a). According to general procedure **B** applied to **3a,** compound **5a** was obtained as a colorless oil (70% yield, 2 steps), using 2.5 equiv ^{t}BuOK. $[\alpha]^{25}_D$ + 7 (c = 0.73, $CHCl_3$); IR (NaCl, cm^{-1}) 3359, 3064, 3032, 2929, 2867, 1699, 1497, 1454, 1402, 1352, 1097, 1070, 1028; ^{1}H NMR (500 MHz, acetone-d_6) δ 2.38−2.45 (m, 1H, CH_2CH═CH_2), 2.65 (broad s, 1H, CH_2CH═CH_2), 3.62−3.64 (m, 1H, H6a), 3.74−3.77 (m, 1H, H6b), 3.97−4.01 (m, 1H, H5), 4.12 (dd, 1H, $J \approx 3$ Hz, $J \approx 6.5$ Hz, H2), 4.21−4.24 (m, 1H, H1), 4.26 (t, 1H, $J \approx 3$ Hz, H3), 4.30−4.32 (m, 1H, H4), 4.46 (d, 1H, $J \approx 12$ Hz, OCH_2Ph), 4.51 (d, 1H, $J \approx 12$ Hz, OCH_2Ph), 4.53−4.74 (m, 6H, OCH_2Ph), 4.94−4.96 (m, 1H, CH_2═CH), 5.01−5.05 (m, 1H, OCH_2Ph), 5.10 (d, 1H, $J \approx 12$ Hz, OCH_2Ph), 5.17 (d, 1H, $J \approx 12$ Hz, OCH_2Ph), 5.75−5.86 (m, 1H, CH═CH_2), 7.27−7.42 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (125 MHz, acetone-d_6) δ 35.2 (*C*H_2CH═CH_2), 62.2−62.9 (*C*1), 66.2 (*C*4), 68.1 (O*C*H_2Ph), 72.7 (*C*6), 73.3, 73.7, 74.3, and 74.5 (O*C*H_2-Ph), 79.6 (*C*5), 82.6 (*C*3), 83.9 (*C*2), 117.4 (CH═*C*H_2), 128.8−131.0 (*C*$H_{Ar's}$), 134.6 (*C*q_{Ar}), 135.1 (*C*q_{Ar}), 137.7 (*C*H═CH_2), 139.9, 139.8, 140.2, 140.4 and 140.7 (*C*q_{Ar}), 158.0 (*C*═O); (+) MS (ESI): m/z = 715.5 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{45}H_{47}NNaO_6$: m/z = 720.3301 $[M + Na]^+$; found : m/z = 720.3296. Anal. Calcd. for $C_{45}H_{47}NO_6$: C, 77.45; H, 6.79; N, 2.01. Found: C, 77.80; H, 6.68; N, 2.09. Note: A sample of mesylate **4a** was purified (PE/AcOEt 85/15 containing a trace of Et_3N); yield: 62%. Then using the general cyclization procedure, compound **5a** was obtained in 55% yield.

3,4,6,7-Tetra-*O*-benzyl-*N*-benzyloxycarbonylamino-2,5-dideoxy-2,5-imino-D-*glycero*-L-*gluco*-heptononitrile (5b). According to general procedure **A** (using TMSCN) and **B** applied to **3b**, compound **5b** was obtained as a colorless oil in 69% yield (3-step yield). $[\alpha]^{25}_D$ +17 (c = 0.66, $CHCl_3$); IR (NaCl, cm^{-1}) 3055, 2987, 2306, 1715, 1454, 1421, 1265, 1099, 1028; ^{1}H NMR (500 MHz, acetone-d_6) δ 3.65−3.67 (m, 1H, H6a), 3.71−3.73 (m, 1H, H6b), 4.05 (br s, 1H, H5), 4.30−4.31 (m, 2H, H3 + H4), 4.43−4.50 (m, 3, H2 + OCH_2Ph), 4.52 (s, 2H, OCH_2Ph), 4.63−4.78 (m, 3H, OCH_2Ph), 4.77 (d, 1H, $J \approx 11.8$ Hz, OCH_2Ph), 5.11 (very br s, 2H, OCH_2Ph), 5.30 (br s, 1H, H1), 7.21−7.42 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (125 MHz, acetone-d_6) δ 53.9−54.2 (*C*1), 66.0 (*C*4), 69.0 (O*C*H_2Ph), 72.3−72.6 (*C*6), 73.0 (O*C*H_2Ph), 74.3 (O*C*H_2Ph), 74.6 (O*C*H_2Ph), 78.5 (*C*5), 82.7−82.9 (*C*2), 83.7−83.8 (*C*3), 117.8 (*C*N), 128.9−130.3 (*C*$H_{Ar's}$), 138.2, 139.1, 139.7, 140.3, and 140.5 (Cq_{Ar}); (+) MS (ESI) : m/z = 700.5 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{43}H_{42}N_2NaO_6$: m/z = 705.2941 $[M + Na]^+$; found : m/z = 705.2944.

Note: Stepwise process from compound **3b** (75.9 mg, 0.108 mmol): mesylated intermediate **4b** was obtained as a colorless oil (74.5 mg, 88%) after purification by flash chromatography (PE/AcOEt 3:1). Compound **5b** was then obtained from **4b** (173 mg, 0.222 mmol) as a colorless oil (100.7 mg, 67%) after purification by flash chromatography (PE/AcOEt 85:15).

4,5,7,8-Tetra-*O*-benzyl-*N*-benzyloxycarbonylamino-2,3,6-trideoxy-3,6-imino-1-*C*-phenyl-D-*glycero*-L-*gluco*-1-octulose (5c). Compound **5c** was prepared from **3c** according to general procedure **B**; mesylation was immediately followed by the cyclization step because intermediate **4c** degrades rapidly. Compound **5c** was obtained as a colorless oil (40%, 2 steps). $[\alpha]^{25}_D$ −2 (c = 0.73, $CHCl_3$); IR (NaCl, cm^{-1}) 3400, 3063, 3032, 2927, 2867, 1699, 1685, 1453, 1408, 1351, 1317, 1266, 1094, 1071, 1027; ^{1}H NMR (500 MHz, acetone-d_6) δ 3.31 (m, 1H, CH_2COPh), 3.55 (m, 2H, H6a + CH_2COPh), 3.71 (br s, 1H, H6b), 3.91 (m, 1H, H5), 4.21−4.28 (m, 3H, H3, H2 + OCH_2Ph), 4.39−4.45 (m, 3H, OCH_2Ph + H4), 4.54−4.65 (m, 4H, OCH_2Ph), 4.70−4.89 (m, 2H, OCH_2Ph + H1), 5.13 (br s, 2H, OCH_2Ph), 6.87−7.58 (m, 30H, C$H_{Ar's}$); ^{13}C NMR (125 MHz, acetone-d_6) δ 39.9 (br, *C*H_2COPh), 59.9−60.4 (C1), 66.5 (C4), 68.0 (O*C*H_2Ph), 72.4−72.6 (C6), 73.85,73.93, 74.4, and 79.3 (O*C*H_2Ph), 82.3 (C3), 83.4−83.5 (*C*2), 127.5−131.2

($CH_{Ar's}$), 134.4−134.8 ($CH_{Ar's}$), 138.7, 138.9, 139.3, 140.0, 140.2, and 140.7 (Cq_{Ar}), 157.6 (C═O), 199.9 (C═O); (+) MS (ESI) : m/z = 794.0 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{50}H_{49}NNaO_7$: m/z = 798.3407 $[M + Na]^+$; found : m/z = 798.3410.

Note: A sample of mesylated intermediate **4c** was purified by flash chromatography (PE/AcOEt 4:1, 70% yield). Cyclization of **4c** according to procedure **B** provided **5c** in 21% yield.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1,4-dideoxy-1,4-imino-1-*C*-(2-oxocyclohexyl)-D-galactitol (5d). According to general procedure **B** applied to compound **3d** (649 mg, 0.841 mmol), mesylated intermediate **4d** was isolated (223.1 mg, 32%) as a colorless oil after purification by flash chromatography (PE/AcOEt 4:1). Cyclization of intermediate **4d** (184 mg, 0.228 mmol) according to procedure **B** afforded compound **5d** as a colorless oil (61.5 mg, 36%) after purification by chromatography (PE/AcOEt 4:1). Alternatively, starting from crude **3d**, compound **5d** was obtained in 36% yield after purification by flash chromatography, without purification of intermediate **4d**. Compound **5d**: $[\alpha]^{25}_D$ +31 (c = 0.94, $CHCl_3$); IR (NaCl, cm^{-1}) 3063, 3031, 2935, 2862, 1703, 1453, 1402, 1351, 1307, 1213, 1093, 1027; ^1H NMR (250 MHz, DMSO-d_6, 80 °C) δ 1.11−1.65 (m, 4H), 1.67−2.31 (m, 4H), 2.69−2.81 (m, 1H, C*H*CO), 3.39−3.79 (m, 3H, 2H6 and H5), 4.02−4.17 (m, 2H, H3 and H2), 4.28−4.39 (m, 2H, H4 and OCH_2Ph), 4.39−4.56 (m, 6H, OCH_2Ph), 4.60−4.74 (m, 2H, OCH_2Ph and H1), 4.96−5.11 (m, 2H, OCH_2Ph), 7.16−7.35 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (62.5 MHz, DMSO-d_6, 80 °C) δ 24.1, 27.8, 31.3, 41.5, and 50.3 (cyclohexyl *C*H2 and *C*H), 58.6 (*C*1), 63.9 (*C*4), 66.0, 70.2, 70.6, 70.7, 71.9, 72.2, and 72.2 (OCH_2Ph, *C*6), 77.8 (*C*5), 82.1 (*C*3 or *C*2), 82.6 (*C*3 or *C*2), 127.0−127.8 ($CH_{Ar's}$), 136.4, 137.5, 137.7, 137.9, and 138.2 (Cq_{Ar}), 156.3 (C═O), 210.5 (C═O); (+) MS (ESI) : m/z = 754.5 $[M + H]^+$, 771.5 $[M + NH_4]^+$.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1,4-dideoxy-1,4-imino-1-*C*-(2-oxocyclopentyl)-D-galactitol (5e). According to general procedure **B** applied to compound **3e** (127 mg, 0.186 mmol), mesylated intermediate **4e** was obtained as a colorless oil (103 mg, 73%) after purification by flash chromatography (PE/AcOEt 7:3). Then compound **5e** was obtained from intermediate **4e** (83 mg, 0.1 mmol) as a colorless oil (18.3 mg, 25%, 67:33 mixture of diastereoisomers at cp-*C*2) after purification by flash chromatography (PE/AcOEt 4:1). IR (NaCl, cm^{-1}) 3019, 2401, 1727, 1720, 1701, 1454, 1406, 1353, 1216, 1093, 1071, 1028; ^1H NMR (500 MHz, acetone-d_6; d1 and d2 for diast. 1 and 2, respectively; cp for cyclopentyl) δ 1.52−2.15 (m, 6H, cp-CH_2), 2.32−2.40 (m, 1H, cp-CH), 3.52 (dd, 0.76H, $J \approx$ 11 and 5.5 Hz, H6a, d1), 3.61 (dd, 0.34H, $J \approx$ 11 and 5 Hz, H6a, d2), 3.72 (dd, 0.76H, $J \approx$ 11 and 3 Hz, H6b, d1), 3.77 (dd, 0.34H, $J \approx$ 11 and 3 Hz, H6b, d2), 4.02−4.06 (m, 1H, H5), 4.07 (d, 0.75H, $J \approx$ 6 Hz, H2, d1), 4.16−4.27 (m, 1.35H, H3 and H2, d2), 4.36−4.52 (m, 5H, OCH_2Ph, H1 and H4), 4.54−4.66 (m, 4H, OCH_2Ph), 4.69−4.80 (m, 1H, OCH_2Ph), 4.97 (d, 0.7H, $J \approx$ 13 Hz, OCH_2Ph), 5.00−5.11 (m, 1.3H, OCH_2-Ph), 7.24−7.44 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (125 MHz, acetone-d_6; d1 and d2 for diast. 1 and 2, respectively; cp for cyclopentyl) δ 21.4 (d1, cp-*C*4), 21.5 (d2, cp-*C*4), 26.7 (d1, cp-*C*3), 28.4 (d2, cp-*C*3), 37.5 (d1, cp-*C*5), 38.9 (d2, cp-*C*5), 49.0−49.2 (cp-*C*2), 62.0−62.3 (*C*1), 66.5 (*C*4), 67.3, 67.4, 71.5, 71.6, 71.68, 71.74, 72.8, 73.0, 73.3, 73.66, and 73.73 (OCH_2Ph, *C*6), 79.1 (d2, *C*5), 79.2 (d1, *C*5), 80.3−80.5 (d1, *C*3), 80.58−80.63 (d2, *C*3), 84.2−84.6 (*C*2), 128.0−129.2 ($CH_{Ar's}$), 138.0, 138.4, 138.89, 138.90, 139.3, 139.6, and 140.3 (Cq_{Ar}), 157.5 (C═O), cp-*C*1 hidden by solvent C═O signal; (+) MS (ESI) : m/z = 762.0 $[M + Na]^+$; HRMS (ESI) calcd for $C_{47}H_{49}NNaO_7$: m/z = 762.3407 $[M + Na]^+$; found : m/z = 762.3416.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1-*C*-but-2-ynyl-1,4-dideoxy-1,4-imino-D-galactitol (5h). According to general procedure **B** applied to compound **3h** (30.1 mg, 0.037 mmol), compound **5h** was obtained as a colorless oil (16.2 mg, 63%) after purification by flash chromatography (PE/AcOEt 9:1) by way of mesylate **4h**. Compound **5h**: $[\alpha]^{25}_D$ +1.5 (c = 1.42, $CHCl_3$); IR (NaCl, cm^{-1}) 3424, 2921, 2861, 1695, 1454, 1403, 1353, 1095, 1070, 1027; ^1H NMR (400 MHz, $CDCl_3$) δ 1.70 (s, 3H, CH_3), 2.28−2.35 (m, 1H, CH_{2a}), 2.53−2.91 (m, 1H, CH_{2b}), 3.37−3.66 (m, 2H, H6), 3.85−3.97 (m, 1H, H5), 4.00−4.10 (m, 2H, H2, H3), 4.18−4.31 (m, 2H, H1, H4), 4.37−4.70 (m, 8H, OCH_2Ph), 5.04−5.20 (m, 2H, OCH_2Ph), 7.10−7.34 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.7 (CH_3), 19.0−20.3 (CH_2), 60.5−61.9 (*C*1), 65.1 (C4), 67.2 (O*C*H_2Ph), 71.4 (O*C*H_2Ph), 71.5−71.8 (*C*6), 73.1, 73.2, and 73.4 (O*C*H_2Ph), 76.4 (C_{alkyne}-CH_3), 77.4 (C_{alkyne}-CH_2), 77.6 (C5), 80.8−81.0 (*C*2 or *C*3), 81.6−82.8 (*C*2 or *C*3), 127.6−128.6 ($CH_{Ar's}$), 136.9, 137.9, 138.1, 138.4, and 138.8 (Cq_{Ar}), 156.8 (C═O); (+) MS (ESI) : m/z = 712.5 $[M + H]^+$; HRMS (ESI) calcd for $C_{46}H_{47}NNaO_6$: m/z = 732.3301 $[M + Na]^+$; found : m/z = 732.3313.

1(*R*)-1-*C*-Allenyl-2,3,5,6-tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1,4-dideoxy-1,4-imino-D-galactitol (5i). According to general procedure **B** applied to compound **3i** (50 mg, 0.063 mmol), compound **5i** was obtained as a colorless oil (33.8 mg, 77%) after purification by flash chromatography (PE/ AcOEt 9:1) by way of mesylate **4i**. Compound **5i**: $[\alpha]^{25}_D$ +28 (c = 0.61, $CHCl_3$); IR (NaCl, cm^{-1}) 3415, 2929, 2867, 1957, 1702, 1497, 1454, 1405, 1353, 1267, 1097; ^1H NMR (400 MHz, $CDCl_3$) δ 3.54−3.75 (m, 2H, H6), 3.95−4.05 (m, 2H, H2 and H5), 4.07−4.20 (m, 2H, H3 and H4), 4.37−4.85 (m, 11H, OCH_2Ph, CH_2= and H1), 4.98−5.28 (m, 3H, OCH_2Ph and C*H*=), 7.18−7.35 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 60.0 (*C*1), 63.5 (*C*4), 67.4, 72.1, 72.2, 73.3, 73.4 (OCH_2Ph, *C*6), 75.8−76.1 (CH_2=), 77.7 (*C*5), 81.9−82.1 (*C*3), 82.9−83.1 (*C*2), 88.2 (*C*H=), 127.6−128.5 ($CH_{Ar's}$), 136.6, 137.8, 138.2, 138.5, and 138.7 (Cq_{Ar}), 156.1 (C═O), 209.3 (=*C*=); (+) MS (ESI) : m/z = 696.5 $[M + H]^+$, 714 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{45}H_{45}NNaO_6$: m/z = 718.31446 $[M + Na]^+$; found : m/z = 718.3143.

General Procedure C: Carbamate Deprotection. Compound **5a** or **5b** (0.056 mmol) and triethylamine (2 μL) were dissolved in ethanol (0.5 mL). The flask was submitted to 3 freeze−pump−thaw cycles and palladium on charcoal (10% Pd on C, 0.1 equiv) was added under argon. The mixture was then placed under hydrogen. After a stirring time of 1.5−3 h at room temperature, the solids were removed by filtration on celite and washed with dichloromethane. Evaporation of the solvents provided a colorless oily product which was homogeneous by NMR.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-1,4-dideoxy-1,4-imino-1-*C*-propyl-D-galactitol (6a). This product was obtained from **5a** (39 mg, 0.056 mmol) as a colorless oil (31.2 mg, 99%). $[\alpha]^{25}_D$ −33 (c = 0.91, $CHCl_3$); IR (NaCl, cm^{-1}) 3055, 2864, 1612, 1454, 1420, 1265, 1108; ^1H NMR (500 MHz, acetone-d_6) δ 0.91 (t, 3H, $J \approx$ 7.4 Hz, CH_3), 1.29−1.46 (m, 2H, CH_2CH$_3$), 1.50−1.57 (m, 1H) and 1.59−1.67 (m, 1H) (CH_2CH$_2$CH$_3$), 2.97 (dt, 1H, $J \approx$ 7 Hz, $J \approx$ 4 Hz, H1), 3.14 (t, 1H, $J \approx$ 4 Hz, H4), 3.72−3.74 (m, 2H, *2*H6), 3.81 (d, 1H, $J \approx$ 4 Hz, H2), 3.81−3.81 (m, 1H, H5), 3.92 (d, 1H, $J \approx$ 4.5 Hz, H3), 4.18−4.25 (m, 0.5H, NH), 4.45−4.55 (m, 5H, OCH_2Ph), 4.60−4.66 (m, 2H, OCH_2Ph), 4.76 (d, 1H, $J \approx$ 11.7 Hz, OCH_2-Ph), 7.21−7.37 (m, 20H, H_{Ar}); ^{13}C NMR (125 MHz, acetone-d_6) δ 15.7 (CH_3), 22.1 (CH_2CH_3), 32.7 ($CH_2CH_2CH_3$), 63.9 (*C*1), 68.8 (*C*4), 72.3, 73.3, and 74.1 (CH_2OPh), 74.5 (*C*6), 74.7 (CH_2OPh), 79.7 (*C*5), 86.4 (*C*2), 86.9 (*C*3), 129.1−130.6 ($CH_{Ar's}$), 130.6 (CH_{Ar}), 133.0 (CH_{Ar}), 140.76, 140.80, 140.8, and 141.0 (Cq_{Ar}); (+) MS (ESI) : m/z = 566.5 $[M + H]^+$; HRMS (ESI) calcd for $C_{37}H_{43}NO_4$: m/z = 566.3270 $[M + H]^+$; found : m/z = 566.3266.

3,4,6,7-Tetra-*O*-benzyl-2,5-dideoxy-2,5-imino-D-*glycero*-L-*gluco*-heptononitrile (6b). Deprotection of **5b** (12 mg, 0.018 mmol) according to general procedure **C** afforded **6b** as colorless oil (9.5 mg, 99%). $[\alpha]^{25}_D$ −7 (c = 0.81, $CHCl_3$); IR (NaCl, cm^{-1}) 3019, 2927, C≡N not visible, 1602, 1455, 1215, 1096; ^1H NMR (500 MHz, $CDCl_3$) δ 3.09 (t, 1H, $J \approx$ 5.3 Hz, H4), 3.54−3.61 (m, 2H, H6), 3.68 (dd, 1H, $J \approx$ 10 Hz, $J \approx$ 5 Hz, H5), 3.81 (dd, 1H, $J \approx$ 5 Hz, $J \approx$ 3.2 Hz, H3), 3.90 (d, 1H, $J \approx$ 5.2 Hz, H1), 4.00 (dd, 1H,

$J \approx 3.1$ Hz, $J \approx 5.2$ Hz, H2), 4.21 (d, 1H, $J \approx 11.7$ Hz, OCH_2Ph), 4.33 (d, 1H, $J \approx 11.7$ Hz, OCH_2Ph), 4.40 (s, 2H, OCH_2Ph), 4.43 (d, 1H, $J \approx 11.7$ Hz, OCH_2Ph), 4.50 (d, 1H, $J \approx 11.8$ Hz, OCH_2-Ph), 4.57 (d, 1H, $J \approx 11.8$ Hz, OCH_2Ph), 4.66 (d, 1H, $J \approx 11.5$ Hz, OCH_2Ph), 7.10−7.31 (m, 20H, C$H_{Ar's}$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 51.4 (*C*1), 65.0 (*C*4), 71.1 (*C*6), 72.3, 72.6, 73.1, and 73.6 (O*C*H_2Ph), 77.3 (*C*5), 83.4 (*C*2), 83.9 (*C*3), 118.0 (CN), 127.8−128.7 (*C*$H_{Ar's}$), 137.1, 137.7, 138.1, and 138.3 (Cq_{Ar}); (+) MS (ESI): m/z = 550.0 [M + H]$^+$; HRMS (ESI) calcd for $C_{35}H_{36}N_2NaO_4$: m/z = 571.2573 [M + Na]$^+$; found : m/z = 571.2572.

General Procedure D: O-Debenzylation. To a 0.01 M solution of benzylated compound (1 equiv) in dry CH_2Cl_2 was added at 0 °C a fresh 1 M solution of BCl_3 in hexane (11.5 equiv). The mixture was stirred overnight at 0 °C, and then the solids formed were dissolved by addition of MeOH (20 mL) and a few drops of water. The reaction mixture was then concentrated under reduced pressure. In some cases, it was found necessary to repeat the reaction with 3 equiv of BCl_3 overnight. In general, purification of the crude final product was performed by flash chromatography on C_{18}-reverse phase silica gel (H_2O/MeOH 1:0 to 4:1), thus providing the debenzylated compound as its hydrochloride salt.

1(*R*)-1-*C*-Allyl-1,4-dideoxy-1,4-imino-D-galactitol (7a). According to general procedure **D,** compound **7a** was prepared from **5a** (134 mg, 0.19 mmol). MeOH and water (5 mL, 20:1) were added to the mixture at the end of the reaction and the solution was quickly filtered through ion-exchange resin (Dowex 1 × 8, OH^- form) which was then washed with MeOH (2 × 20 mL) and water (10 mL). Purification of the crude product by flash chromatography on silica gel (CH_2Cl_2/MeOH 7:3 to 3:2) provided compound **7a** (12.7 mg, 33%) as a brown product. $[\alpha]^{25}_D$ −30 (c = 1.21, MeOH); ^{1}H NMR (CD_3OD, 500 MHz) δ 2.48−2.54 (m, 1H) and 2.60−2.66 (m, 1H)(allyl-CH_2), 3.37 (dd, 1H, $J \approx 8$ Hz, $J \approx 2.5$ Hz, H4), 3.57 (td, 1H, $J \approx 3$ and 7.5 Hz, H1), 3.65 (dd, 1H, $J \approx 5$ and 11.5 Hz, H6a), 3.72 (dd, 1H, $J \approx 4.5$ and 11.5 Hz, H6b), 3.85−3.90 (m, 1H, H5), 3.98 (dd, 1H, $J \approx 1$ and 3 Hz, H2), 4.08 (dd, 1H, $J \approx 1$ and 2.5 Hz, H3), 5.18 (dd, 1H, $J \approx 1.5$ and 10 Hz, =CH_aH_b), 5.27 (dd, 1H, $J \approx 1.5$ and 17 Hz, =CH_aH_b), 5.89 (m, 1H, =CH); ^{13}C NMR (CD_3OD, 125 MHz) δ 31.5 (*C*H_2CH=), 63.1 (*C*1), 64.8 (*C*6), 70.3 (*C*4), 71.7 (*C*5), 77.0 (*C*2), 78.8 (*C*3), 119.0 (=*C*H_2), 134.5 (=*C*H); (+) MS (ESI) : m/z = 204.0 [M + H]$^+$; HRMS (ESI) calcd for $C_9H_{18}NO_4$: m/z = 204.1236 [M + H]$^+$, found : m/z = 204.1239.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1,4-dideoxy-1-*C*-(3-diethylphosphono-2-propen-1-yl)-1,4-imino-D-galactitol (9). To a solution of **5a** (172.4 mg, 0.248 mmol) in dry CH_2Cl_2 (4.1 mL) was added dropwise commercial diethyl vinylphosphonate (76.8 μL, 0.495 mmol, 2 equiv). The flask was submitted to 3 freeze−pump−thaw cycles and placed under Ar. Then Hoveyda-Grubbs catalyst (7.8 mg, 5%) was added and the 3 freeze−pump−thaw-argon cycles were repeated. The reaction mixture was stirred for 12 h at 40 °C, then another addition of Hoveyda-Grubbs catalyst (7.8 mg, 5%) was made. After an additional stirring time of 12 h at 40 °C, the reaction mixture was concentrated under reduced pressure. Excess diethyl vinylphosphonate was removed from the brown residue by coevaporation with toluene. Purification by flash chromatography (CH_2Cl_2/MeOH 99:1) afforded compound **9** (154.9 mg, 75%) as a brown oily product. IR (NaCl, cm^{-1}) 3063, 3031, 2981, 2867, 1701, 1454, 1402, 1353, 1267, 1247, 1216, 1099, 1059, 1027; ^{1}H NMR (400 MHz, DMSO-d_6, 80 °C; $J_{H,H}$ coupling constants were measured on a ^{31}P-decoupled spectrum) δ 1.22 (t, 6H, $J \approx 7$ Hz, CH_3), 2.48−2.53 (m, 1H) and 2.58−2.66 (m, 1H) (CH_2CH=CH), 3.57 (dd, 1H, $J \approx 5.9$ Hz, $J \approx 10.9$ Hz, H6a), 3.70 (dd, 1H, $J \approx 2.8$ Hz, $J \approx 10.9$ Hz, H6b), 3.87 (m, 1H, H5), 3.92 (quint, 4H, $J \approx 7.1$ Hz, CH_2CH$_3$), 4.09−4.13 (m, 1H, H2), 4.16−4.19 (m, 2H, H3, H4), 4.29 (q, 1H, $J \approx 7.2$ Hz, H1), 4.43−4.68 (m, 8H, OCH_2Ph), 5.09 (broad s, 2H, OCH_2Ph), 5.61−5.70 (dd, 1H, $J \approx 17$ Hz, J_{H-P}∼21.3 Hz, PC*H*=CH), 6.58−6.71 (ddt, 1H, $J \approx 6.6$ Hz, $J \approx 17$ Hz, J_{H-P}∼21.8 Hz, PCH=C*H*), 7.28−7.37 (m, 25H, C$H_{Ar's}$); ^{13}C NMR (125 MHz, DMSO-d_6, 80 °C) δ 16.5 (d, *C*H$_3$), 34.2 (d, $J \approx 21.6$ Hz, *C*H$_2$CH=CHP), 59.8 (*C*1), 61.4 (d, CH$_3$*C*H$_2$O), 64.4 (*C*2), 66.9 (O*C*H$_2$Ph), 71.4 (O*C*H$_2$Ph), 71.8 (*C*6), 72.4 (O*C*H$_2$Ph), 72.9 (O*C*H$_2$Ph), 73.1 (O*C*H$_2$Ph), 78.2 (*C*5), 81.9 (*C*3 or *C*4), 82.5 (*C*3 or *C*4), 118.8 (PC*H*=CH$_2$ $J_{C,P}$∼186 Hz, measured in $CDCl_3$), 127.7−128.7 (*C*$H_{Ar's}$), 137.8−138.2 (Cq_{Ar}), 150.0 (CH$_2$*C*H=CH), 156.4 (C=O); ^{31}P NMR (202 MHz, $CDCl_3$) δ 18.25; (+) MS (ESI): m/z = 835 [M + H]$^+$, 856 [M + Na]$^+$; HRMS (ESI) calcd for $C_{49}H_{56}NNaO_9P$: m/z = 856.3590 [M + Na]$^+$, found : m/z = 856.3583. Anal. Calcd. for $C_{49}H_{56}NO_9P$: C, 70.57; H, 6.77; N, 1.68. Found: C, 70.15; H, 6.70; N, 1.71.

1,4-Bis-[1(*R*)-2,3,5,6-tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1,4-dideoxy-1,4-imino-D-galactit-1-yl)-2-butene (10). A solution of **5a** (209 mg, 0.3 mmol) in dry CH_2Cl_2 (3.5 mL) was submitted to 3 freeze−pump−thaw cycles and placed under Ar. Then Hoveyda-Grubbs catalyst (9.4 mg, 5%) was added and the 3 freeze−pump−thaw-argon cycles were repeated. The green reaction medium was stirred overnight at 40 °C and then the brown mixture was concentrated under reduced pressure. Purification by flash chromatography (PE/AcOEt 85:15) provided compound **10** (108.1 mg, 53%) as a green oily product. IR (NaCl, cm^{-1}) 3442, 3052, 3031, 1695, 1454, 1403, 1265, 1096, 1069; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17−2.31 (m, 2H, CH_2CH=), 2.37−2.77 (m, 2H, CH_2CH=), 3.39−3.68 (m, 4H, H6), 3.84−3.96 (m, 4H, H5, H2), 3.99−4.14 (m, 4H, H1, H3), 4.20 (dd, 2H, $J \approx 2.4$ and 6.8 Hz, H4), 4.28−4.56 (m, 14H, OCH_2Ph), 4.58−4.70 (m, 2H, OCH_2Ph), 4.97−5.13 (m, 4H, OCH_2Ph), 5.39−5.50 (m, 2H, C*H*=), 7.16−7.29 (m, 50H, C$H_{Ar's}$); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 27.7 (*C*H_2CH=), 32.4, (*C*H_2CH=), 60.6−61.6 (*C*1), 64.1 (*C*4), 64.4 (*C*4), 67.06 (*C*6), 67.10 (*C*6), 71.5, 71.6, 72.0−72.1, 72.4, 73.15, 73.21, and 73.3 (O*C*H_2Ph), 77.4 (*C*5), 77.9 (*C*5), 80.8 (*C*3), 81.12−81.15 (*C*3), 82.3−82.8 (*C*2), 127.5−128.5 (*C*$H_{Ar's}$), 129.1 (CH$_2$*C*H=), 129.2 (CH$_2$*C*H=), 136.82, 136.84, 137.8, 138.1, 138.2, 138.4, 138.7, and 138.8 (Cq_{Ar}), 156.8 (C=O); (+) MS (ESI) : m/z = 1385.0 [M + NH_4]$^+$; HRMS (ESI) calcd for $C_{88}H_{90}N_2O_{12}Na$: m/z = 1389.63915 [M + Na]$^+$; found : m/z = 1389.6389. Anal. Calcd. for $C_{88}H_{90}N_2O_{12}$: C, 77.28; H, 6.63; N, 2.05. Found: C, 77.06; H, 6.65; N, 1.98.

1(*R*)-1,4-Dideoxy-1-*C*-(3-diethylphosphono-2-propen-1-yl)-1,4-imino-D-galactitol (11). Compound **11** was obtained according to procedure **D**, starting from compound **9** (220 mg, 0.263 mmol). Purification by C_{18}-reverse phase silica gel chromatography (H_2O/MeOH 1:0 to 9:1) afforded the hydrochloride salt of **11** (98.8 mg, 74%) as a colorless foamy product. $[\alpha]^{25}_D$ −20 (c = 1.46, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 1.33 (t, 6H, $J \approx 7$ Hz, CH_3), 2.74−2.80 (m, 1H) and 2.85−2.91 (m, 1H)(CH_2CH=CH), 3.44−3.48 (m, 1H, H4), 3.66 (dd, 1H, $J \approx 4.5$ Hz, $J \approx 11.5$ Hz, H6a), 3.71−3.77 (m, 2H, H1 and H6b), 3.86−3.90 (m, 1H, H5), 4.01 (d, 1H, $J \approx 2.5$ Hz, H2), 4.06−4.13 (m, 5H, H3 and CH_2CH$_3$), 6.02 (dd, 1H, $J \approx 17$ Hz, J_{H-P}∼20.8 Hz, PC*H*=CH), 6.75 (ddt, 1H, $J \approx 7$ Hz, $J \approx 17$ Hz, J_{H-P}∼21.5 Hz, PCH=C*H*); ^{13}C NMR (125 MHz, CD_3OD) δ 16.6 (*C*H$_3$), 16.7 (*C*H$_3$), 31.4 (d, $J \approx 23.7$ Hz, *C*H$_2$-CH=CHP), 62.1 (*C*1), 63.5 (CH$_3$*C*H$_2$O), 63.6 (CH$_3$*C*H$_2$O), 64.7 (*C*6), 70.9 (*C*4), 71.5 (*C*5), 76.9 (*C*2), 78.1 (*C*3), 121.8 (d, $J \approx$ 186.5 Hz, PC*H*=CH$_2$), 148.9 (d, $J \approx 5.3$ Hz, CH$_2$*C*H=CH); ^{31}P NMR (202 MHz, CD_3OD) δ 17.84 (s); (+) MS (ESI): m/z = 340.5 [M + H]$^+$, 362.5 [M + Na]$^+$; HRMS (ESI) calcd for $C_{13}H_{26}NNaO_7P$: m/z = 362.13446 [M + Na]$^+$; found : m/z = 362.1340. Anal. Calcd. for $C_{13}H_{27}ClNO_7P+2H_2O$: C, 39.65; H, 7.42; N, 3.56; Cl, 9.00. Found: C, 39.75; H, 6.94; N, 3.4; Cl, 9.66.

General Procedure E: Preparation of Free Phosphonic Acids. To a 0.1 M solution of ethyl phosphonate (**11** or **19**) (1 equiv) in dry MeCN was added $BrSiMe_3$ (10 eq) at room temperature. The mixture was stirred for the indicated time. The mixture was then diluted with MeOH (15 mL) and concentrated under reduced pressure. The dilution and evaporation process was repeated twice. The residue was then taken up with water and the mixture extracted with CH_2Cl_2 to remove traces of less polar organic compounds. The aqueous phase was concentrated under reduced pressure.

Chromatography of the crude product on C_{18}-reversed phase silica gel (H_2O/MeOH 1:0 to 4:1) provided free phosphonic acids.

(1*R*)-1,4-Dideoxy-1-*C*-(3-phosphono-2-propen-1-yl)-1,4-imino-D-galactitol (12). Compound **12** was obtained as a brownish foam (10.7 mg, 59%) from **11** (20 mg, 0.05 mmol) according to general procedure **E** (reaction time: 64 h). ^{1}H NMR (400 MHz, CD_3OD) δ 2.70−2.77 (m, 1H) and 2.81−2.89 (m, 1H) (C*H*$_2$CH=CH), 3.47 (dd, 1H, $J \approx 2.4$ and 8.8 Hz, H4), 3.67 (dd, 1H, $J \approx 8$ Hz, $J \approx 11.6$ Hz, H6a), 3.70−3.77 (m, 2H, H1 and H6b), 3.88−3.92 (m, 1H, H5), 4.02−4.07 (m, 1H, H2), 4.13 (m, 1H, $J \approx 2.4$ Hz, H3), 6.01−6.11 (m, 1H, PC*H*=CH), 6.54−6.70 (m, 1H, PCH=C*H*); ^{13}C NMR (100 MHz, CD_3OD) δ 31.1 (d, $J \approx 23$ Hz, *C*H$_2$CH=CHP), 62.3 (*C*1), 64.6 (*C*6), 70.7 (*C*4), 71.5 (*C*5), 76.7 (*C*2), 78.1 (*C*3), 117.5 (P*C*H=CH$_2$), 144.7 (CH$_2$*C*H=CH); ^{31}P NMR (162 MHz, CD_3OD) δ 14.54 (s); HRMS (ESI) calcd for $C_{13}H_{26}NNaO_7P$: m/z = 362.13446 [M + Na]$^+$; found : m/z = 362.1340.

1,4-Bis-[1(*R*)-1,4-dideoxy-1,4-imino-D-galactit-1-yl]-2-butene (13). Compound **13** was prepared by the debenzylation procedure **D**, starting from compound **10** (196 mg, 0.143 mmol). Compound **13** was obtained as a colorless foam, as its hydrochloride salt (62 mg, 96%) and as a mixture of *Z*/*E* isomers (1:2). ^{1}H NMR (250 MHz, CD_3OD) δ 2.48−2.83 (m, 4H, C*H*$_2$CH=), 3.40−3.53 (m, 2H, H4), 3.57−3.81 (m, 6H, H1, 2H6), 3.86−3.94 (m, 2H, H5), 3.98−4.07 (m, 2H, H2), 4.07−4.18 (m, 2H, H3), 5.63−5.69 (m, 0.7H, CH=, *Z*-isomer), 5.71−5.80 (m, 1.3H, CH=, *E*-isomer); ^{13}C NMR (62.5 MHz, CD_3OD) δ 24.9 (*C*H$_2$CH=, *Z*), 29.9 (*C*H$_2$-CH=, *E*), 63.25 (C1, *Z*), 63.30 (C1, *E*), 64.6 (C6), 70.56 (C4, *E*), 70.60 (C4, *Z*), 71.45 (C5, *Z*), 71.49 (C5, *E*), 76.6 (*C*2, *Z*), 76.7 (*C*2, *E*), 78.2 (C3, *E*), 78.3 (C3, *Z*), 128.5 (CH=, *Z*), 130.0 (CH=, *E*); (+) MS (ESI) : m/z = 379.5 [M + H]$^+$; HRMS (ESI) calcd for $C_{16}H_{30}N_2NaO_8$: m/z = 401.18999 [M + Na]$^+$, found : m/z = 401.1898

Ethyl (2′,3′-*O*-isopropylideneuridin-5′-yl) vinylphosphonate (17). To a solution of diethyl vinylphosphonate (377 μL, 2.44 mmol) in dry CH_2Cl_2 (10 mL) was added oxalyl chloride (230 μL, 2.68 mmol, 1.1 equiv) under Ar. After stirring overnight at room temperature, the mixture was stirred at 35 °C for 24 h and then concentrated under reduced pressure. Ethyl vinylphosphonyl chloride was thus obtained with a conversion of 94% (^{1}H NMR integration) as a colorless oily product. This reagent was used without further purification because it was air and moisture sensitive. To a solution of ethyl vinylphosphonyl chloride (340 mg, 2.2 mmol) in dry CH_2Cl_2 (11 mL) under Ar were added 2′,3′-*O*-isopropylideneuridine (940 mg, 3.30 mmol, 1.5 equiv) and Et_3N (618 μL, 4.39 mmol, 2 equiv). The purple mixture was stirred for 36 h at 35 °C, then the reaction was quenched by adding water (2 mL). Compound **17** was extracted with CH_2Cl_2 (3×), the organic layers were combined and dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The pink foam thus obtained was purified by flash chromatography (CH_2Cl_2/MeOH 99:1 to 96:4). Compound **17** was obtained as a white foam (540 mg, 61% from commercial diethyl vinylphosphonate) and as a 1:1 mixture of *P*-stereoisomers (d1 and d2). IR (NaCl, cm^{-1}) 3466, 3169, 3057, 2989, 2940, 1694, 1633, 1457, 1383, 1271, 1235, 1159, 1067, 1019; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.21−1.27 (m, 6H, C*H*$_3$ isopropylidene + C*H*$_3$CH$_2$O), 1.48 (s, 3H, C*H*$_3$ isopropylidene), 3.98−4.11 (dquint, 2H, $J \approx 7.5$ Hz, CH$_3$C*H*$_2$O d1 and d2), 4.24−4.29 (m, 2H, H5′), 4.32−4.40 (m, 1H, H4′), 4.77−4.80 (m, 1H, H3′), 4.86 (dd, 1H, $J \approx 6.25$ Hz, H2′ d1 and d2), 5.64 (d, 1H, $J \approx 8$ Hz, H5), 5.73 (dd, 1H, $J \approx 4.75$ Hz, H1′ d1 and d2), 5.87−6.39 (m, 3H, C*H*$_2$=CHP + CH$_2$=C*H*P d1 and d2), 7.39 (t, 1H, $J \approx 8.25$ Hz, H6 d1 and d2), 10.44 (broad s, 1H, NH); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 16.0, 16.1 (*C*H$_3$, d1 and d2), 26.0 and 26.9 (CH$_3$, isopropylidene), 62.2, 62.3 (CH$_3$*C*H$_2$O d1 and d2), 64.9−65.0 (m, C5′ d1 and d2), 80.5, 80.6 (C3′ d1 and d2), 84.2, 84.3 (*C*2′ d1 and d2), 85.3 (d, $J_{C-P} \sim 11.3$ Hz, C4′ d1), 85.5 (d, $J_{C-P} \sim 11.3$ Hz, C4′ d2), 93.4, 93.7 (C1′ d1 and d2), 102.2, 102.3 (C5, d1 and d2), 114.15, 114.18 (Cq isopropylidene, d1 and d2), 124.8 (d, $J_{C-P} \sim 183$ Hz, P*C*H=CH$_2$ d1), 124.9 (d, $J_{C-P} \sim 183$ Hz, P*C*H=CH$_2$ d2), 136.4 (PCH=*C*H$_2$), 141.8, 141.9 (C6, d1 and d2), 150.13, 150.15 (*C*2, d1 and d2), 163.7 (C4); ^{31}P NMR (202 MHz, $CDCl_3$) δ 17.83 (s), 18.0 (s); (+) MS (ESI) : m/z = 420.0 [M + NH$_4$]$^+$; HRMS (ESI) : calcd for $C_{16}H_{23}N_2NaO_8P$: m/z = 425.1090 [M + Na]$^+$; found : m/z = 425.1092.

1(*R*)-2,3,5,6-Tetra-*O*-benzyl-*N*-benzyloxycarbonyl-1,4-dideoxy-1-*C*-{3-[(ethyl)(2′,3′-*O*-isopropylideneuridin-5′-yl)phosphono]-2-propen-1-yl}-1,4-imino-D-galactitol (18). To a solution of compound **5a** (115 mg, 0.165 mmol) in dry CH_2Cl_2 (2.75 mL) was added compound **17** (133 mg, 0.33 mmol, 2 equiv). The flask was then submitted to 3 freeze−pump−thaw cycles and placed under Ar. Then Hoveyda-Grubbs catalyst (5.2 mg, 5%) was added and the 3 freeze−pump−thaw-argon cycles were repeated. The reaction medium was stirred for 24 h at 40 °C, then a second addition of Hoveyda-Grubbs catalyst (5.2 mg, 5%) was performed. After 20 h stirring time at 40 °C, the reaction mixture was concentrated under reduced pressure. The brownish residue was dried by coevaporation with toluene. Purification by flash chromatography (CH_2Cl_2/MeOH 99:1 to 98:2) provided compound **18** (107.5 mg, 61%) as a brown oily product (1:1 mixture of *P*-stereoisomers, d1 and d2). IR (NaCl, cm^{-1}) 3032, 2988, 2935, 2249, 1695, 1455, 1266, 1215, 1158, 1095, 1068, 1028; ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 1.22 (t, 3H, $J \approx 6.3$ Hz, OCH$_2$C*H*$_3$, d1), 1.24 (t, 3H, $J \approx 6.3$ Hz, OCH$_2$C*H*$_3$ d2), 1.34 (s, 3H) and 1.54 (s, 3H, C*H*$_3$ isopropylidene), 2.48−2.53 (m, 1H, C*H*$_a$CH=CHP), 2.61−2.68 (m, 1H, C*H*$_b$CH=CHP), 3.58 (dd, $J \approx 5.8$ Hz, $J \approx 10.9$ Hz, 1H, H6a), 3.69 (dd, $J \approx 3.24$ Hz, $J \approx 10.9$ Hz, 1H, H6b), 3.88−3.94 (m, 1H, H5), 3.93−4.00 (m, 2H, OC*H*$_2$CH$_3$), 4.08−4.13 (m, 2H, H3 + H5′), 4.18 (m, 2H, H2 + H4), 4.22 (q, 1H, $J \approx 5.2$ Hz, H4′), 4.27−4.33 (m, 1H, H1), 4.46 (d, 1H, $J \approx 5.1$ Hz, OC*H*$_2$Ph), 4.50−4.59 (m, 6H, OC*H*$_2$Ph), 4.66 (d, 1H, $J \approx 11.6$ Hz, OC*H*$_2$Ph), 4.82 (dd, 1H, $J \approx 4$ Hz, $J \approx 6.4$ Hz, H3′), 5.02 (m, 1H, H2′), 5.10 (broad s, 2H, OC*H*$_2$Ph), 5.61 (d, 1H, $J \approx 8$ Hz, H5”), 5.66−5.74 (m, 1H, CH=C*H*P), 5.86−5.87 (m, 1H, H1′), 6.62−6.76 (m, 1H, C*H*=CHP), 7.27−7.39 (m, 25H, C*H*$_{Ar's}$), 7.64 (dd, 1H, $J \approx 8$ Hz, H6”); ^{13}C NMR (125 MHz, DMSO-d_6, 80 °C) δ 16.28 (*C*H$_3$), 16.32 (*C*H$_3$), 25.6 and 27.3 (2 *C*H$_3$ isopropylidene), 34.1 (d, $J_{C-P} \sim 22.1$ Hz, *C*H$_2$CH=CHP), 59.66, 59.71 (C-1, d1 and d2), 61.66, 61.71 (O*C*H$_2$CH$_3$, d1 and d2), 64.26, 64.31 (*C*2, d1 and d2), 64.96, 65.00 (C5′, d1 and d2), 66.8 (O*C*H$_2$-Ph), 71.2, 71.5, 72.3, 72.7, 72.9 (C6 + 4 O*C*H$_2$Ph), 78.0 (C5), 81.1 (C3′), 81.8 (C4), 82.3 (C-3), 83.9 (*C*2′), 85.2 (m, C4′), 92.65, 92.68 (C-1′, d1 and d2), 102.3 (C5”), 113.8 (Cq isopropylidene), 118.5 (d, $J_{C-P} \sim 185.6$ Hz, CH=*C*HP d1), 118.7 (d, $J_{C-P} \sim 185.6$ Hz, CH=*C*HP d2), 127.5−128.5 (*C*H$_{Ar's}$), 137.1, 138.0, 138.5, 138.7, and 138.9 (Cq$_{Ar}$), 142.4 (C-6”), 150.6 (d, $J_{C-P} \sim 21.6$ Hz, *C*H=CHP), 156.2 (C=O), 163.2 (C=O); ^{31}P NMR (202 MHz, $CDCl_3$) δ 17.94 (s), 18.01 (s); (+) MS (ESI) : m/z = 1095.5 [M + Na]$^+$; HRMS (ESI) calcd for $C_{59}H_{66}N_3NaO_{14}P$: m/z = 1094.4180 [M + Na]$^+$; found : m/z = 1094.4175. Anal. Calcd. for $C_{59}H_{66}N_3O_{14}P$: C, 66.09; H, 6.20; N, 3.92. Found: C, 66.07; H, 6.20; N, 3.79.

1(*R*)-1,4-Dideoxy-1-*C*-{3-[(ethyl)(uridin-5′-yl)phosphono]-2-propen-1-yl}-1,4-imino-D-galactitol (19). To a solution of **18** (79 mg, 0.073 mmol) in dry CH_2Cl_2 (2.5 mL) was added BCl_3 (862 μL, 735 mmol, 100 equiv) at 0 °C under argon. The reaction mixture was stirred overnight at 0 °C, then it was diluted by the addition of CH_2Cl_2 (2.5 mL) and the solids formed during the reaction were dissolved by the addition of MeOH (15 mL) and a few drops of water. The reaction mixture was then concentrated under reduced pressure. MeOH and water (5 mL, 20:1) were added and the solution was quickly filtered through ion-exchange resin (Dowex 1 × 8, OH$^-$ form) which was then washed with MeOH (2 × 20 mL) and water (10 mL). Purification of the crude product by flash chromatography on C_{18}-reversed phase silica gel (H_2O/*i*-PrOH 1:0 to 7:3) provided compound **19** (20.2 mg, 52%) as a white foam (1:1 mixture of *P*-stereoisomers). ^{1}H NMR (500 MHz, CD_3OD, d1 and d2 for *P*-epimers) δ 1.35 (t, 3H, $J \approx 6.3$ Hz, OCH$_2$C*H*$_3$, d1), 1.36 (t, 3H, $J \approx 6.3$ Hz, OCH$_2$C*H*$_3$, d2), 2.70−2.78 (m, 1H) and 2.83−2.88 (m, 1H)(C*H*$_2$CH=CHP), 3.40 (m, 1H, H4), 3.63−

3.74 (m, 3H, H1, 2H6), 3.85−3.88 (m, 1H, H5), 3.99−4.00 (m, 1H, H2), 4.09 (brs, 1H, H3), 4.12−4.18 (m, 4H, OCH_2CH$_3$ + H2′), 4.19−4.21 (m, 1H, H4′), 4.22−4.26 (m, 1H, H5′a), 4.30−4.34 (m, 1H, H5′b), 5.71 (d, 1H, $J \approx 8$ Hz, H5”), 5.83 (dd, 1H, $J \approx 3.9$ Hz, $J \approx 6.1$ Hz, H1′), 6.01−6.09 (m, 1H, CH=C*H*P), 6.68−6.77 (m, 1H, C*H*=CHP), 7.72 (dd, 1H, $J \approx 8$ Hz, H6” d1 and d2); ^{13}C NMR (125 MHz, CD$_3$OD) δ 16.65, 16.70 (*C*H$_3$, d1 and d2), 32.0 (d, J_{C-P}∼22.1 Hz, *C*H$_2$CH=CHP), 61.8 (C1), 63.9, 64.0 (O*C*H$_2$CH$_3$, d1 and d2), 64.8 (*C*2), 66.2−66.3 (m, C5′), 70.5 (C4), 70.9 (C3′), 71.7 (C5), 74.99, 75.02 (*C*2′, d1 and d2), 77.1 (C3), 78.6, 78.7 (*C*2, d1 and d2), 83.55, 83.60 (C4′, d1 and d2), 91.8, 91.9 (C1′, d1 and d2), 102.9 (C5”), 120.7 (d, J_{C-P}∼187.3 Hz, CH=*C*HP), 120.8 (d, J_{C-P}∼187.1 Hz, CH=*C*HP), 142.49, 142.54 (C-6”, d1 and d2), 150.5 (m, *C*H=CHP), 152.2 (C=O), 166.0 (C=O); ^{31}P NMR (202 MHz, CD$_3$OD) δ 18.35 (s), 18.53 (s); (+) MS (ESI) : $m/z = 538.5$ [M + H]$^+$; HRMS (ESI) calcd for $C_{20}H_{33}N_3O_{12}P$: $m/z = 538.1802$ [M + H]$^+$; found : $m/z = 538.1800$. Calcd for $C_{20}H_{32}N_3NaO_{12}P$: $m/z = 560.1621$ [M + Na]$^+$; found : $m/z = 560.1622$.

Procedure for 19·HCl. Debenzylation of phosphonate **18** (149 mg, 0.139 mmol) according to general procedure **D** afforded compound **19** as its hydrochloride salt (62.6 mg, 78%). Anal. Calcd. for $C_{20}H_{33}ClN_3O_{12}P+2H_2O$: C, 39.38; H, 6.11; N, 6.89; Cl, 5.81. Found: C, 39.27; H, 6.29; N, 6.53; Cl, 5.80.

1(*R*)-1,4-Dideoxy-1-*C*-{3-[(uridin-5′-yl)phosphono]-2-propen-1-yl}-1,4-imino-D-galactitol (20). Compound **20** (8 mg, 36%) was obtained as a white foam from **19** (21.9 mg, 0.038 mmol) according to general procedure **E** (stirring time: 3 d). $[\alpha]^{25}_D$ −2 ($c = 0.49$, MeOH); ^{1}H NMR (400 MHz, CD$_3$OD) δ 2.58−2.80 (m, 2H, CH_2-CH=CHP), 3.42 (dd, 1H, $J \approx 2.4$ Hz, $J \approx 8.4$ Hz, H4), 3.62−3.77 (m, 3H, H1 and 2H6), 3.85−3.90 (m, 1H, H5), 3.98−4.12 (m, 5H), 4.19−4.23 (m, 2H), 5.79 (d, 1H, $J \approx 8$ Hz, H5”), 5.89−6.01 (m, 2H, H1 and CH=C*H*P), 6.36−6.50 (m, 1H, C*H*=CHP), 8.01 (d, 1H, $J \approx 8$ Hz, H6”); ^{13}C NMR (100 MHz, CD$_3$OD) δ 31.4 (d, J_{C-P}∼21.6 Hz, *C*H$_2$CH=CHP), 62.8 (C1), 64.5 (d, J_{C-P}∼4.6 Hz, C5′), 64.7 (m, C6), 70.7 (C4), 71.5 (C3′ or *C*2′), 71.7 (C5), 75.6 (*C*2′ or C3′), 77.0 (*C*2), 78.3 (C3), 85.1 (d, J_{C-P}∼8.2 Hz, C4′), 90.0 (C1′), 103.0 (C5”), 128.4 (d, J_{C-P}∼175 Hz, CH=*C*HP), 142.1 (*C*H=CHP), 142.6 (C6”), 152.6 (C=O), 166.2 (C=O); ^{31}P NMR (162 MHz, CD$_3$OD) δ 12.05 (s); (+) MS (ESI): $m/z = 532.5$ [M + Na]$^+$; HRMS (ESI) calcd for $C_{18}H_{28}N_3NaO_{12}P$: $m/z = 532.13083$ [M + Na]$^+$; found : $m/z = 538.1306$.

Inhibition Assay. Inhibition assays of UGM by the new compounds were performed as previously described.[15b]

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Supporting Information Available: Experimental procedures and characterization data for compounds **2**, **2′**, **3f**, **3f′**, **3g**, **8**, **14**, **15**, **16**, and copies of NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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