Carba-D,L-allal- and -D,L-galactal-derived vinyl *N*-nosyl aziridines as useful tools for the synthesis of 4-deoxy-4-(*N*-nosylamino)-2,3-unsaturated-5*a*-carbasugars

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Abstract: The novel carba-D,L-allal- and carba-D,L-galactal-derived vinyl *N*-nosyl aziridines were prepared and the regio- and stereoselective behavior in opening reactions with *O*- and *N*-nucleophiles examined. The carbaglycosylating ability of the novel aziridines**,** as deduced by the amount of *1,4-addition products* (1,4-regioselectivity) obtained in the acid-catalyzed methanolysis taken as a model reaction, is similar or superior to that observed with the corresponding carba-D,L-allal- and -D,L-galactal-derived vinyl epoxides, respectively. In all *1,2*- and *1,4-addition products* obtained, a *N*-nosylamino group is regio- and stereoselectively introduced at the C(4) carbon of a 1,2- or 2,3-unsaturated carbasugar, susceptible to further elaborations toward aminocyclitol derivatives. The stereoselective synthesis of the corresponding, enantiomerically pure carba-D,L-allal- and -D,L-galactal-derived vinyl *N*-acetyl aziridines is also described.

Keywords: Vinyl aziridines, 4-(*N*-nosylamino)-carbasugars, Carbaglycosylation, Regioselectivity.

1.Introduction

Carbasugars, a particular family of cyclitols, are compounds structurally related to carbohydrates with the only difference being the replacement of the endocyclic oxygen with a methylene group.[1] This structural modification is responsible for an increased chemical stability and makes carbasugars valuable mimics of the corresponding carbohydrates.[2]

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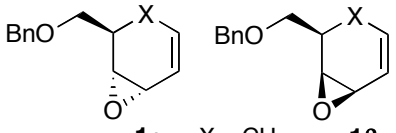
Within the carbasugar family, aminocyclitols, also regarded as amino carbasugars, can be found in nature in several families of natural and clinically important antibiotics.[3] Moreover, aminocyclitols represent interesting scaffolds in drug discovery. In fact, these structures are present in currently used therapeutic agents,[4] and turn out to be attractive substrates for targeting many key pathways implicated in disorders such as diabetes, viral infections and cancer.[5]

Although the synthesis of amino carbasugars has been investigated and reviewed extensively,[5,6] new versatile methodologies for their preparation still represent an interesting challenge in synthetic carbohydrate chemistry.

Following our experience with vinyl epoxides[7] and *N*-activated aziridines,[7e,8] we herein present a stereoselective synthesis of 2,3-unsaturated-4-(*N*-protected-amino) carbasugars by using carba-D,L-glycal-derived vinyl *N*-nosyl aziridines, as suitable precursors.

Recently, racemic and enantiopure vinyl epoxides **1α** and **1β**,[9] the carba analogs of the previously studied D-allal-and D-galactal-derived vinyl epoxides **2α** and **2β**,[7c-f,h-l] were synthesized and their regio- and stereoselective behavior examined in addition reactions with several *O*-, *C*-, *N*- and *S*-nucleophiles. In particular, by using MeOH as a model *O*-nucleophile, the possibility of considering these epoxides suitable for the stereoselective construction of carba-*O*-glycosides and/or mixed carba-oligo-saccharides was checked. For such an application, a complete or high 1,4-regioselective behavior with associated high stereoselectivity, in the opening reactions, is required. This behavior, defined as carbaglycosylating ability, is determined by the total amount of *1,4-addition products* obtained.[9]

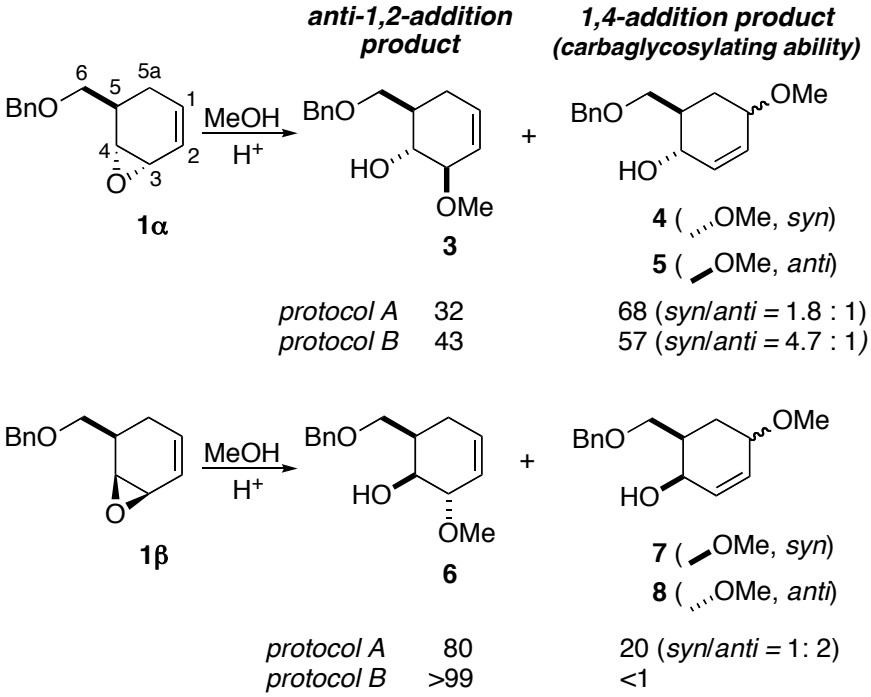


1α X = CH_2 **1β**

2α X = O **2β**

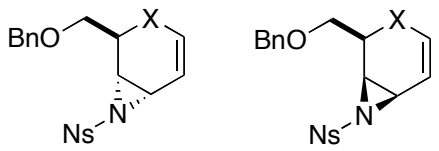
The results obtained after acid methanolysis indicated an interesting carbaglycosylating ability for epoxide **1α**, with moderate syn-stereoselectivity, as shown by 68% (1.8:1 *syn*/*anti* ratio) and 57% 1,4-regioselectivity (4.7:1 *syn*/*anti* ratio) under *protocol A* (0.2 N H_2SO_4/MeOH) and synthetically more interesting *protocol B* reaction conditions (MeOH, 6 equiv, in 10^{-2} N TsOH/CH_2Cl_2), respectively.[9a,10] In this framework, diastereoisomeric epoxide **1β** turned out to be a very poor carbaglycosyl donor, as shown by the low 1,4-regioselectivity (20%) observed under the corresponding *protocol A*, and by the complete anti-1,2-regioselectivity (>99%) found under the corresponding *protocol B* reaction conditions. These results and the structures of all the addition

products obtained in the acid methanolysis of epoxides **1α** and **1β** (methoxy alcohols **3**-**8**), are shown in Scheme 1.[9a,10]



Scheme 1. Regio- and stereoselectivity of vinyl carba epoxides **1α** and **1β** in the acid methanolysis under *protocol A* and *protocol B* reaction conditions.

As an extension of our interest toward glycal-derived systems and their corresponding carba analogues, and looking for new, effective carbaglycosyl donors, our attention was directed to the diastereoisomeric carba-D,L-allal- and -D,L-galactal-derived vinyl *N*-nosyl aziridines **9α-Ns** and **9β-Ns**, the carba analogs of the corresponding, previously studied D-allal- and D-galactal-derived *N*-nosyl aziridines **10α-Ns** and **10β-Ns**.[7e,8c]



9α-Ns X = CH_2 **9β-Ns**
10α-Ns X = O **10β-Ns**

The examination of the regio- and stereoselective behavior in nucleophilic opening reactions could indicate whether aziridines **9α-Ns** and **9β-Ns** are effective carbaglycosyl donors with

simultaneous, completely regio- and stereoselective introduction of a –(*N*-nosylamino) group at C(4)-carbon of a 2,3-unsaturated carbasugar system as shown in **11**, with high levels of syn-1,4-stereoselectivity, if possible**,** when alcohols (ROH) are used as carbaglycosyl acceptors (Scheme 2). The presence of the double bond and the easy deprotection of the –(*N*-nosylamino) group,[8c] could make carbapyranosides **11** suitable for further elaborations toward biologically interesting aminocyclitols,[3-6] through a new synthetic approach (Scheme 2, where only *N*-nosyl aziridine **9α-Ns** is shown, for simplicity).

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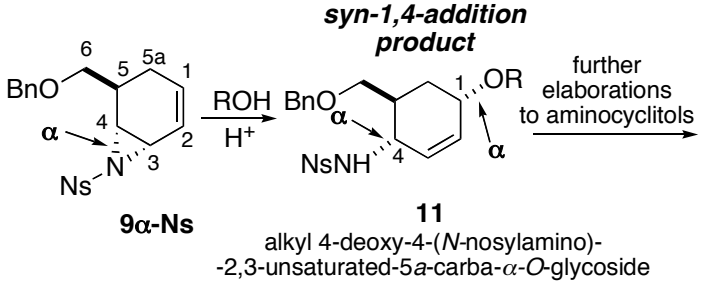
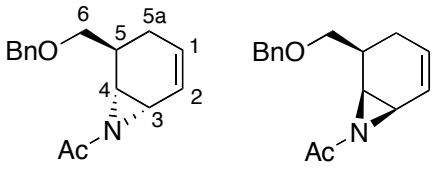


Scheme 2. The conceivable behavior of aziridine **9α-Ns** as a carbaglycosyl donor in the acid alcoholysis, with complete 1,4-syn-stereoselectivity and simultaneous complete regio- and stereoselective introduction of a –(*N*-nosylamino) group at C(4) carbon of a 2,3-unsaturated carbasugar.

In this preliminary examination of their regio- and stereoselective behavior in nucleophilic addition reactions, *N*-nosyl aziridines **9α-Ns** and **9β-Ns** were prepared in a racemic form. However, in view of a possible use of these systems for the construction of compounds of biological interest, an enantioselective route to both aziridine systems, in the form of *N*-acetyl analogs, as (3*S*,4*R*,5*S*)-**9α-Ac** and (3*R*,4*S*,5*S*)-**9β-Ac**, has been disclosed, also.

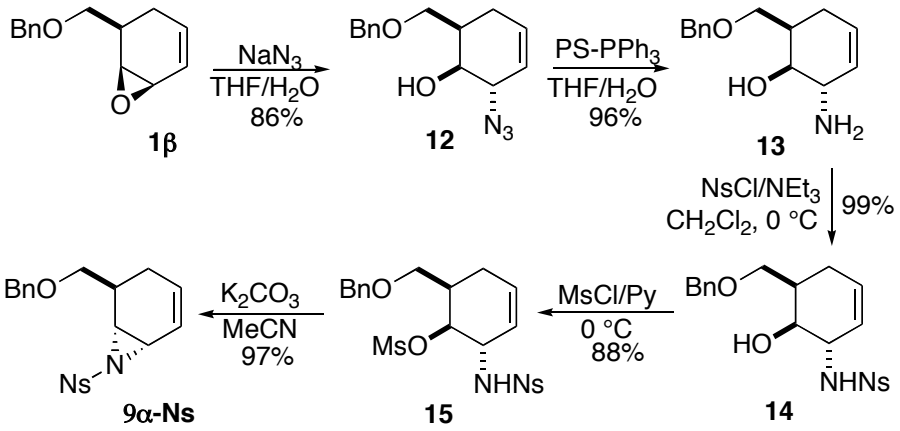


(3*S*,4*R*,5*S*)-**9α-Ac** (3*R*,4*S*,5*S*)-**9β-Ac**

2. Results and discussion

The stereoselective synthesis of vinyl aziridines **9α-Ns** and **9β-Ns** was carried out by means of the same protocol starting from azidolysis of the corresponding epoxide with the opposite configuration **1β** and **1α**, respectively.

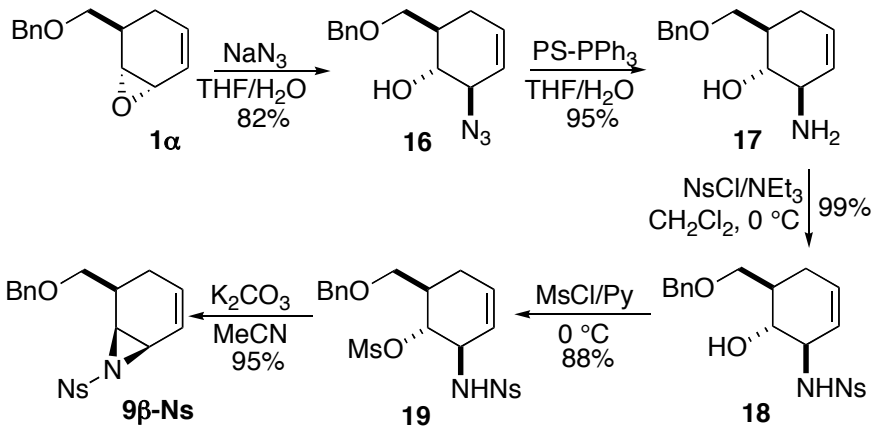
For the synthesis of aziridine **9α-Ns**, the azidolysis of epoxide **1β** by NaN_3 in a 1:1 THF/H_2O mixture[11] turned out to be completely 1,2-regio- and anti-stereoselective affording *trans* 3,4-azido alcohol **12** as the only reaction product (Scheme 3)**.**[12]



Scheme 3. Synthesis of vinyl *N*-nosyl aziridine **9α-Ns**.

trans 3,4-Azido alcohol **12** was reduced by polimer-supported PPh_3 (PS-PPh_3, Aldrich)[8b] in a heterogeneous phase (20:1 THF/H_2O) to the corresponding *trans* 3,4-amino alcohol **13**, which was obtained in good yield (96%) and was sufficiently pure to be directly used in the next step. Regioselective *N*-nosylation of the amino group of **13** by a NsCl/NEt_3/CH_2Cl_2 protocol afforded *N*-nosyl derivative **14**. Subsequent *O*-mesylation by MsCl/Py of the free -OH functionality gave *trans* *N*-nosyl-*O*-mesyl derivative **15**. The treatment of mesylate **15** under basic conditions (K_2CO_3/MeCN) gave the cyclization to the desired aziridine **9α-Ns** which was obtained with a good overall yield (69%), through a 5 step sequence, starting from epoxide **1β** (Scheme 3).

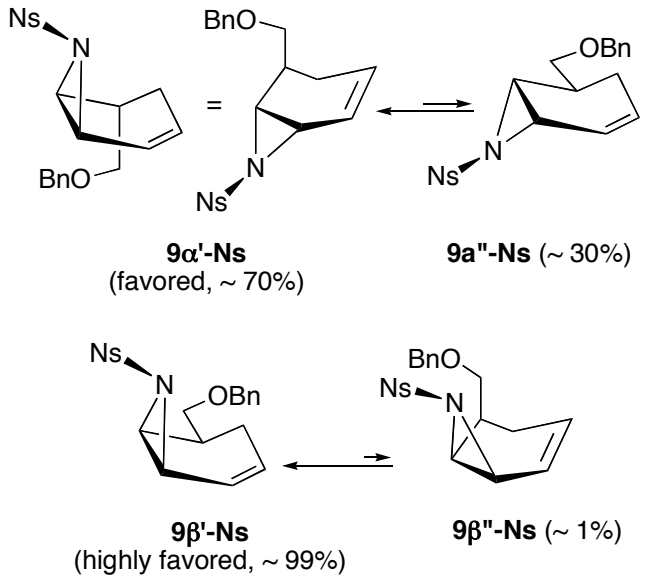
The treatment of epoxide **1α** with NaN_3 in 1:1 THF/H_2O[11] mixture afforded *trans* 3,4-azido alcohol **16** as the only reaction product.[12] Reduction of azido alcohol **16** to *trans* 3,4-amino alcohol **17** by PS-PPh_3 in THF/H_2O,[8b] followed by regioselective *N*-nosylation to *N*-nosyl derivative **18** and subsequent *O*-mesylation by MsCl/Py protocol led to *trans* *N*-nosyl-*O*-mesyl derivative **19**. Base-catalyzed (K_2CO_3/MeCN) cyclization of **20** afforded pure aziridine **9β-Ns** (64% overall yield through 5 steps starting from epoxide **1α**, Scheme 4).



Scheme 4. Synthesis of vinyl *N*-nosyl aziridine **9β-Ns**.

Aziridines **9α-Ns** and **9β-Ns**, even if prudentially stored at -15°C, turned out to be sufficiently stable also at room temperature.

A theoretical conformational study (performed with DF, density functional theory calculation, in vacuum) carried out on simplified models (see Supplemetary data, sections 4.1, 4.2 and 4.3), has indicated that *N*-nosyl aziridine **9α-Ns** largely exists as the favored conformer **9α'-Ns** (nearly a 70:30 equilibrium between the two conformers **9α'-Ns** and **9α"-Ns**) whereas aziridine **9β-Ns** practically exists as the only, highly favored, conformer **9β'-Ns** (about 99 %, Scheme 5). It is worth noting that the favored conformer **9α'-Ns** in aziridine **9α-Ns** and the highly favored conformer **9β'-Ns** in aziridine **9β-Ns** have the same ring conformation with the side chain (–CH_2OBn) axial in **9α'-Ns** and equatorial in **9β'-Ns** (Scheme 5).



Scheme 5. Theoretical conformational analysis of *N*-nosyl aziridines **9α-Ns** and **9β-Ns**.

2.1. Regio- and stereoselective behavior of N-nosyl aziridines ***9α-Ns*** *and* ***9β-Ns*** *in nucleophilic addition reactions*

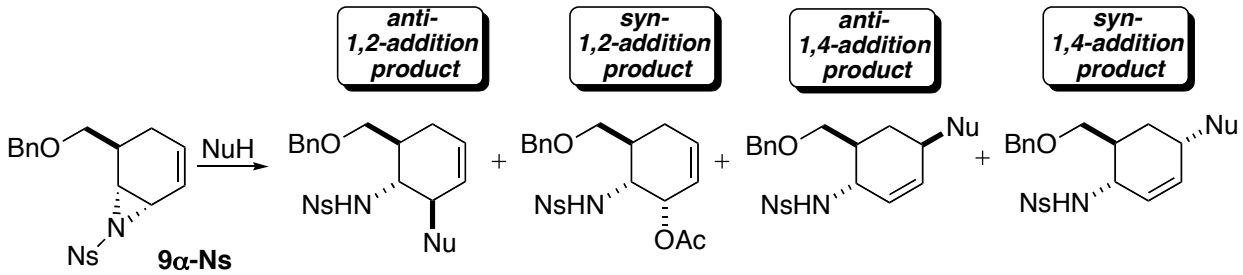
Methanolysis and acetolysis reactions were carried out under acidic conditions (*protocol A* and *B* reaction conditions)[10] and aminolysis reactions were carried out in the presence of a Lewis acid as $Sc(OTf)_3$ (*protocol A*).[10] Conversely, alkaline acetolysis (AcONa/DMF) and azidolysis reactions (NaN_3/THF-H_2O) (*protocol B*)[10] did not necessitate any catalyst. Alkaline methanolysis (MeONa/MeOH) afforded only complex reaction mixtures. The results will be presented in the following sections.

2.1.1. Regio- and stereoselective behavior of N-nosyl aziridines ***9α-Ns*** *and* ***9β-Ns*** *in nucleophilic addition reactions of MeOH (O-nucleophile) under acid conditions*

The regio- and stereochemical behavior of aziridine **9α-Ns** in the acid methanolysis turned out to be strictly dependent on the reaction conditions and, in particular, on the aziridine:MeOH ratio.

In fact, when the methanolysis was carried out using 0.2 N H_2SO_4 solution in MeOH, that is in the presence of a large amount of the nucleophile (*protocol A* reaction conditions, see Table 1),[10] the reaction did not show regio- and/or stereoselectivity affording a 38:30:32 mixture of *trans*-3-methoxy-4-(*N*-nosylamino)-derivative **20** (*anti-1,2-addition product*), *trans*-1-methoxy-4-(*N*-nosylamino)-derivative **21** (*anti-1,4-addtion product*) and *cis*-1-methoxy-4-(*N*-nosylamino)-derivative **22** (*syn-1,4-addition product*) (^{1}H NMR spectroscopy) (entry 1, Table 1). When the methanolysis of aziridine **9α-Ns** was performed using a $2.5 \cdot 10^{-3}$ N TsOH solution in CH_2Cl_2 containing a drastically reduced amount of MeOH in such a way that aziridine:TsOH:MeOH ratio = 1:0.1:6 (*protocol B* reaction conditions),[10] a completely 1,2-regio- and *anti*-stereoselective behavior was observed, with the exclusive production of *anti-1,2-addition product* **20** (entry 2, Table 1).

Table 1. Regio- and stereoselectivity of acid methanolysis and acetolysis of aziridine **9α-Ns**, under *protocol A* and *B* reaction conditions.[a,b]



NuH = MeOH/H$^+$, Nu = OMe **20**
AcOH/H$^+$ Nu = OAc **23**

24

21
25

22
26

Entry	Reagents	*anti-1,2-addition product*	*syn1,2-addition product*	*anti-1,4-addition product*	*syn-1,4-addition product*
1	MeOH/0.2 N H_2SO_4[a]	38	-	____30____ **62**[c]	____32____
2	MeOH (6 equiv) $2.5\cdot10^{-3}$ N TsOH/ CH_2Cl_2[b]	>99	-	-	
3	MeOH (6 equiv) $2.5\cdot10^{-3}$ N TsOH 1:1 CH_2Cl_2/[bimim][BF_4][b]	>99	-	-	
4	AcOH/0.2 N H_2SO_4 [a]	8	22	____45____ **70** [c]	_____25____
5	AcOH (6 equiv) $2.5\cdot10^{-3}$ N TsOH/CH_2Cl_2[b]	11	29	____19____ **60** [c]	_____41___
6	AcONa (4 equiv)/DMF[b]	>99	-	-	

[a] *Protocol A* reaction conditions: the nucleophile (MeOH or AcOH) is the reaction solvent in the presence of the acid (H_2SO_4).

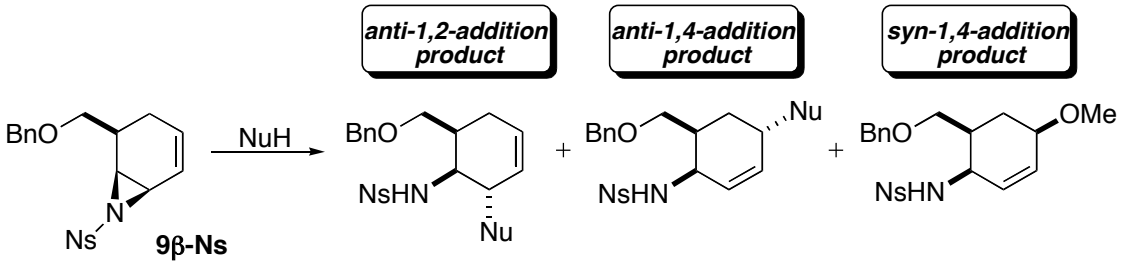
[b] *Protocol B* reaction conditions: aziridine:nucleophile (MeOH or AcOH) ratio = 1:6 in CH_2Cl_2 or 1:1 CH_2Cl_2/[bimim][BF_4], as the reaction solvent, in the presence of the acid (TsOH, 0.1 eq); aziridine:AcONa ratio = 1: 4 in the alkaline acetolysis in DMF.

[c] Total amount of *1,4-addition products* (carbaglycosylating ability).

Aziridine **9β-Ns** showed a similar regio- and stereochemical behavior but, surprisingly, obtained under diametrically opposed reaction conditions. Actually, under *protocol B* reaction conditions,[10] a 40:35:25 mixture of *trans*-3-methoxy-4-(*N*-nosylamino)-derivative **27** (*anti-1,2-addition product*), *trans*-1-methoxy-4-(*N*-nosylamino)-derivative **28** (*anti-1,4-addtion product*) and

cis-1-methoxy-4-(*N*-nosylamino)-derivative **29** (*syn-1,4-addition product*) (^{1}H NMR spectroscopy) was obtained indicating a non-regioselective behavior (entry 2, Table 2). On the contrary, when the methanolysis reaction of aziridine **9β-Ns** was repeated under *protocol A* reaction conditions,[10] a complete 1,2-regio- and *anti*-stereoselective addition was observed with the isolation of *anti-1,2-addition product* **27**, as the only reaction product (entry 1, Table 2).

Table 2. Regio- and stereoselectivity of acid methanolysis and acetolysis of aziridine **9β-Ns** under *protocol A* and *B* reaction conditions.[a,b]



Entry	Reagents	*anti-1,2-addition product*	*anti-1,4-addition product*	*syn-1,4-addition product*
1	MeOH/0.2N H_2SO_4[a]	>99	-	-
2	MeOH (6 equiv) $2.5\cdot10^{-3}$ N TsOH/ CH_2Cl_2[b]	40	35	25
			60[c]	
3	MeOH (6 equiv) $2.5\cdot10^{-3}$ N TsOH 1:1 CH_2Cl_2/[bimim][BF_4][b]	40	28	32
			60[c]	
4	AcOH/0.2 N H_2SO_4 [a]	36	64	-
			64[c]	
5	AcOH (6 equiv) $2.5\cdot10^{-3}$ N TsOH/CH_2Cl_2[b]	30	70	-
			70[c]	
6	AcONa (4 equiv)/DMF[b]	>99	-	

[a] *Protocol A* reaction conditions: the nucleophile (MeOH or AcOH) is the reaction solvent in the presence of the acid (H_2SO_4).

[b] *Protocol B* reaction conditions: aziridine:nucleophile (MeOH or AcOH) ratio = 1:6 in CH_2Cl_2 or 1:1 CH_2Cl_2/[bimim][BF_4], as the reaction solvent, in the presence of the acid (TsOH, 0.1 eq); aziridine:AcONa ratio = 1: 4 in the alkaline acetolysis in DMF.

[c] Total amount of *1,4-addition products* (carbaglycosylating ability).

The reason for the different regiochemical behavior of aziridines **9α-Ns** and **9β-Ns** under the same reaction conditions (see entries 1 and 2, Tables 1 and 2) can be rationalized by considering the influence that the different acid reaction conditions (*protocol A* and *B*) could have on the conformational equilibrium in the two aziridines.

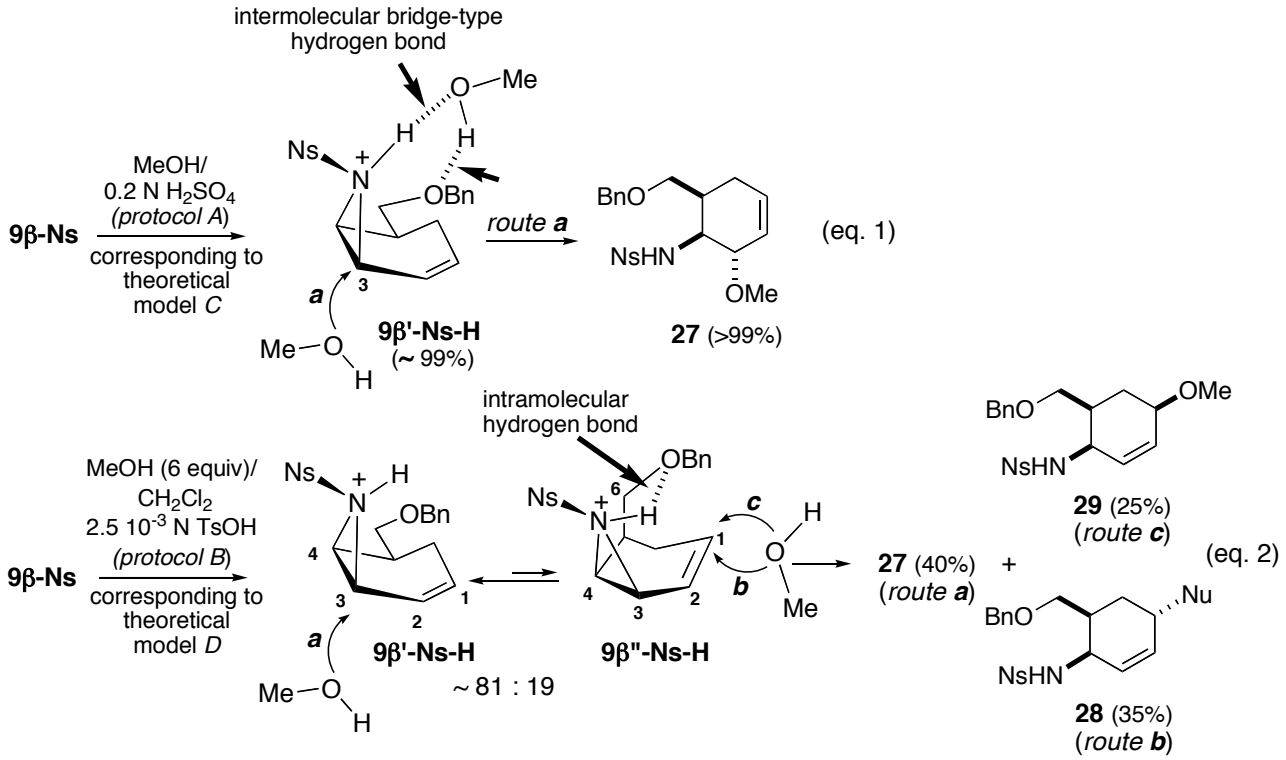
A DFT theoretical conformational study on protonated aziridine **9β-Ns-H**, the species likely present under acid conditions, carried out with and without the solvent, simulated in an explicit way by one molecule of MeOH (theoretical model *C* and *D*, respectively), has indicated, first of all, that the protonation occurs inside the ring with the bulky –Ns group outside (Schemes 6 and 7, and Supplementary data, sections 4.3 and 4.4).

In the presence of one molecule of MeOH (theoretical model *C*), the most favored minimum energy structure shows the presence of two bridge-type intermolecular hydrogen bonds in which MeOH is contemporarily hydrogen-bonded to the protonated aziridine nitrogen and the oxygen of the 6-OBn functionality of the cis-disposed equatorial side chain. The occurrence of these hydrogen bonds determines the exclusive presence of the highly favored conformer **9β'-Ns-H** with the side –CH_2OBn chain equatorial (about 99%, Scheme 6 and Supplementary data, section 4.4).[13]

On the contrary, in the absence of MeOH (theoretical model *D*), the occurrence of an intramolecular hydrogen bond between the protonated aziridine and the oxygen of the 6-OBn group of the cis-disposed axial side chain, possible only through conformer **9β"-Ns-H**, makes this conformer consistently present at the equilibrium (**9β'-Ns-H** : **9β"-Ns-H** conformers ratio nearly 81: 19, Scheme 6 and Supplementary data, section 4.3).

By admitting that theoretical models *C* (presence of one molecule of MeOH) and *D* (absence of MeOH) correspond to experimental *protocol A* (presence of a large amount of MeOH, solvent of the reaction)[10] and *protocol B* reaction conditions (presence of only a small amount of MeOH, 6 equiv, in CH_2Cl_2, the reaction solvent),[10] respectively, nucleophilic attack by MeOH under *protocol A* (corresponding to model *C*) necessarily occurs at aziridine C(3)-carbon of the only present conformer **9β'-Ns-H** through a sterically unhindered, highly favored trans diaxial opening of the aziridine ring (*route **a***, eq. 1, Scheme 6).[14] In this way, the corresponding *anti-1,2-addition product* **27**, is reasonably the only reaction product, as experimentally observed (>99%, entry 1, Table 2).

On the other hand, under *protocol B* (corresponding to theoretical model *D*) nucleophilic attack can reasonably occur on both conformers **9β'-Ns-H** and **9β"-Ns-H**, consistently present at the equilibrium (eq. 2, Scheme 6). In this framework, even if nucleophilic attack at the aziridine C(3)-carbon of conformer **9β'-Ns-H** remains highly favored (a trans-diaxial opening process, *route **a***),[14] nucleophilic attack on conformer **9β"-Ns-H**, necessarily occurring at the more reactive vinyl C(1)-carbon in a conjugated fashion through *routes **b*** and ***c***, becomes competitive and a 40:35:25 mixture of *anti-1,2-* **27** (*route **a***), *anti-1,4-* **28** (*route **b***), and *syn-1,4-addition product* **29** (*route **c***) is reasonably obtained, as found experimentally (eq. 2, Scheme 6 and entry 2, Table 2).[15] Nucleophilic attack at C(3)-aziridine carbon of protonated conformer **3β"-Ns-H** does not occur because it corresponds to a stereoelectronically disfavored trans-diequatorial ring opening process.[14,16,17]



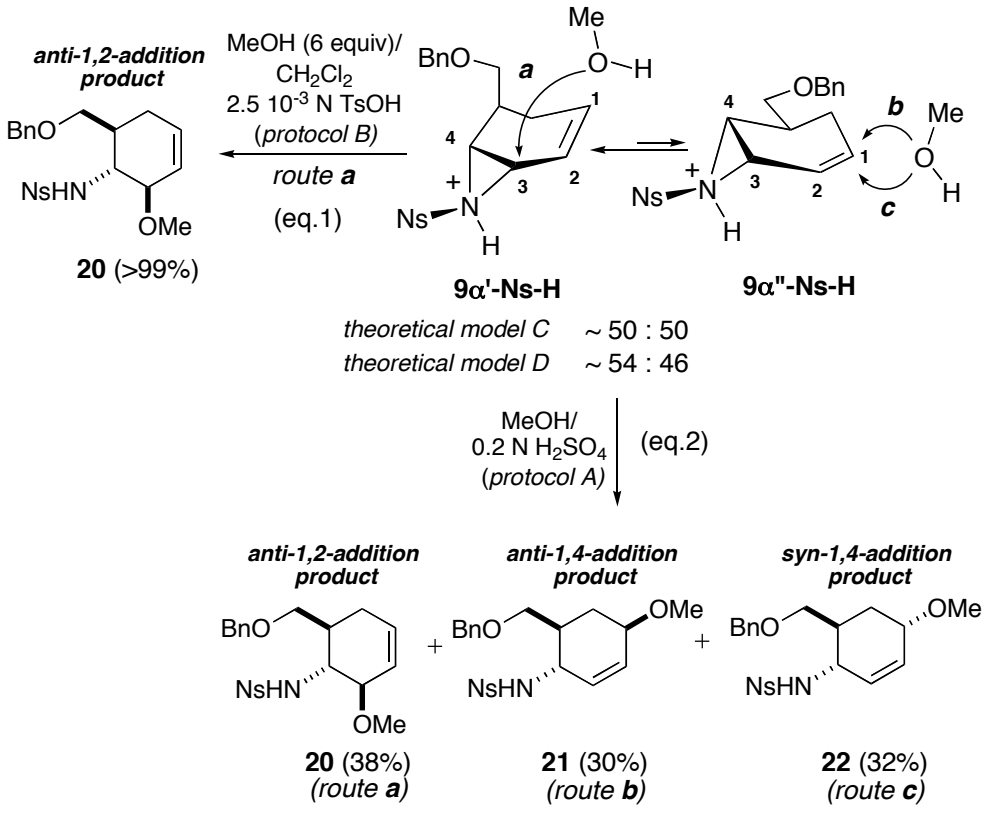
Scheme 6. Theoretical conformational analysis of protonated aziridine **9β-Ns-H** in the presence (theoretical model *C*) and absence of one molecule of MeOH (theoretical model *D*), and regio- and stereoselectivity of aziridine **9β-Ns** in acid methanolysis under *protocol A* and *B* reaction conditions.

In the case of protonated aziridine **9α-Ns-H**, due to the trans relationship between protonated aziridine nitrogen and $-CH_2OBn$ side chain, no intramolecular hydrogen bond of the type observed

with aziridine **9β-Ns-H** under acid conditions can occur. As a consequence, almost the same theoretical protonated conformer **9α'-Ns-H** : **9α"-Ns-H** ratio has been found both in the presence (nearly 50:50, theoretical model *C*) and in the absence of one molecule of MeOH (nearly 54:46, theoretical model *D*) (Scheme 7 and Supplementary data, sections 4.5 and 4.6).[18]

On the basis of the conformational analysis, the stereo- and regioselective result observed in the acid methanolysis of aziridine **9α-Ns** can be explained by the amount of nucleophile present in the reaction mixture and the different reactivity of the two conformers **9α'-Ns-H** and **9α"-Ns-H**.

In the presence of only a small amount of MeOH (*protocol B*), nucleophilic attack occurs only at the aziridine C(3)-carbon of the protonated conformer **3α'-Ns-H**, due to the possibility of having a highly favored trans-diaxial ring opening process (*route **a***, eq. 1, Scheme 7 and entry 2, Table 1).[14] As a consequence, *anti-1,2-addition product* **20** is the only reaction product, as observed. On the contrary, when the reaction is carried out in the presence of a large amount of nucleophile (MeOH as solvent, *protocol A*), nucleophilic attack in a conjugated fashion at the vinyl C(1)-carbon of the protonated aziridine **9α"-Ns-H**, equally from the α and β direction, becomes competitive to nucleophilc attack at the C(3)-carbon of conformer **9α'-Ns-H**. As a consequence a mixture of all the possible addition products is obtained: *anti-1,2-* **20** (38%, *route **a***), *anti-1,4-* **21** (30%, *route **b***) and *syn-1,4-addition product* **22** (32%, *route **c***) (eq. 2, Scheme 7 and entry 1, Table 1).[14,17]



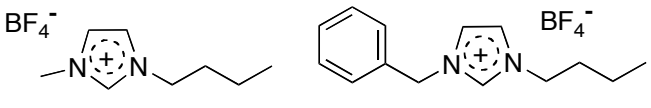
Scheme 7. Theoretical conformational analysis of protonated aziridine **9α-Ns-H** in the presence (theoretical model *C*) and absence of one molecule of MeOH (theoretical model *D*) and regio- and stereoselectivity of aziridine **9α-Ns** in acid methanolysis under *protocol A* and *B* reaction conditions.

The results obtained with MeOH, as a model *O*-nucleophile, indicate that *N*-nosyl aziridines **9α-Ns** and **9β-Ns** are not completely 1,4-regioselective, under the experimented reaction conditions, in presence of the nucleophile as a solvent or as a reagent (*protocol A* and *B*). However, the overall amount of *1,4-addition products* (*anti*- and *syn*-adducts) is sufficiently high (62 and 60% from **9α-Ns** and **9β-Ns**, entries 1 and 2, Tables 1 and 2, respectively) to make aziridines **9α-Ns** and **9β-Ns** be considered useful in carbaglycosylating processes. Moreover, a comparison with the corresponding results obtained with epoxides **1α** and **1β** indicates that the carbaglycosylating ability of aziridines **9α-Ns** (62%, *protocol A*) and **9β-Ns** (60%, *protocol B*) is similar and superior to the maximum value obtained with the corresponding epoxides **1α** (68%, *protocol A* and 57%, *protocol B*) and **1β** (20%, *protocol A*), respectively.[9a,19]

*2.2. Acid methanolysis of epoxides **1α** and **1β** and N-nosyl aziridines **9α-Ns** and **9β-Ns** in the presence of an ionic liquid (IL)*

On the basis of the above described results, some different conditions able to influence positively the regioselectivity of the methanolysis reactions toward *1,4-addition products*, and thus the carbaglycosylating ability, not only with aziridines **9α-Ns** and **9β-Ns**, but also with the related, previously studied, epoxides **1α** and **1β**,[9] were tried. Considering that an increase in the 1,4-addition process could reasonably be obtained by an opening process characterized by a more diffused carbocation-like intermediate, the use of an ionic liquid (IL) was envisaged.[20]

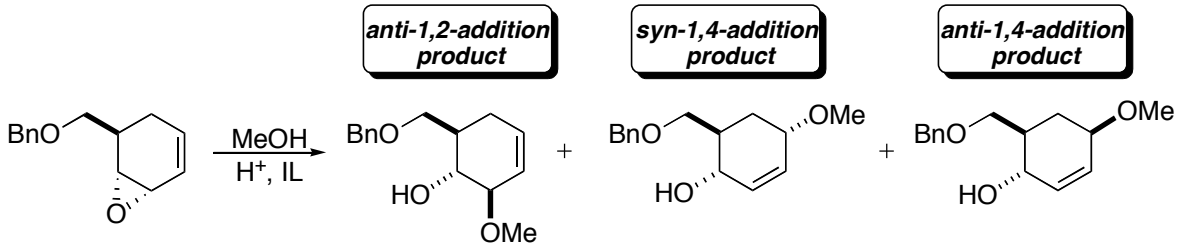
Two different ILs, butylmethylimidazolium tetrafluoroborate ([bmim][BF_4]) (**IL1**) and benzylbutylimidazolium tetrafluoroborate ([bzbim][BF_4]) (**IL2**), soluble in organic solvents, were checked.



IL1 **IL2**

IL1 and **IL2** were used as solvent or cosolvent in different acidic reaction conditions (10^{-2} H_2SO_4 or $2.5 \cdot 10^{-3}$ N TsOH). The nucleophile (MeOH) was present in a large amount when cosolvent of the reaction with IL (1:1 MeOH/IL ratio, *protocol A*), or only in a controlled amount (6 equiv) with respect to the epoxide, when IL or 1:1 IL/CH_2Cl_2 mixture was the solvent of the reaction (*protocol B*). The result obtained with epoxides **1α** and **1β** are reported in Tables 3 and 4, respectively, where the results previously obtained under standard conditions are also reported (entries 1 and 2 , Tables 3 and 4).[9a]

Table 3. Regio- and stereoselectivity, with indication of the carbaglycosylating ability, of epoxide **1α** in acid methanolysis reactions (*protocol A* and *B)* under standard conditions and in the presence of an IL.



Entry	Reaction conditions	*anti-1,2-addition product*	*anti-1,4-addition product*	*syn-1,4-addition product*
1	0.2 N H_2SO_4 /MeOH (*A*)[a,b]	32	44	24
			68[c]	
2	MeOH (6 equiv) in 10^{-2} N TsOH/CH_2Cl_2 (*B*) [a,b]	43	47	10
			57 [c]	
3	10^{-2} N H_2SO_4 in 1:1 MeOH/[bmim][BF_4] (*A*) [b]	31	33	36
			69 [c]	
4	MeOH (6 equiv) in $2.5 \cdot 10^{-3}$ N TsOH / 1:1 CH_2Cl_2/[bmim][BF_4] (*B*) [b]	20	76	4
			80 [c]	
5	MeOH (6 equiv) in $2.5 \cdot 10^{-3}$ TsOH/[bmim][BF_4] (*B*) [b]	25	45	30
			75 [c]	

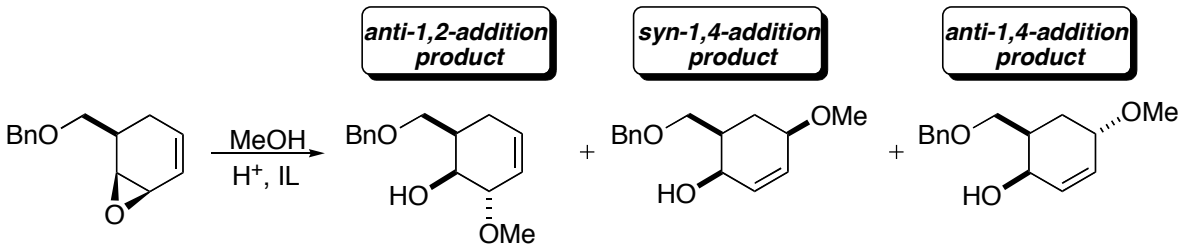
6	10^{-2} N H_2SO_4 in 1:1 MeOH/[bzbim][BF_4] (*A*) [b]	50	30	20 **50** [c]

[a] See ref. 9a.

[b] (*A*): *protocol A*; (*B*): *protocol B* (see Tables 1 and 2 and ref. 10).

[c] Total amount of *1,4-addition products* (carbaglycosylating ability).

Table 4. Regio- and stereoselectivity, with indication of the carbaglycosylating ability, of epoxide **1β** in acid methanolysis reactions (*protocol A* and *B)* under standard conditions and in the presence of an IL.



Entry	Reaction conditions	*anti-1,2-addition product*	*anti-1,4-addition product*	*syn-1,4-addition product*
1	0.2 N H_2SO_4 /MeOH (*A*)[a,b]	80	5	15 **20** [c]
2	MeOH (6 equiv) in 10^{-2} N TsOH/CH_2Cl_2 (*B*)[a,b]	>99	-	-
3	10^{-2} N H_2SO_4 in 1:1 MeOH/[bmim][BF_4] (*A*) [b]	67	23	10 **33** [c]
4	MeOH (6 equiv) in $2.5 \cdot 10^{-3}$ N TsOH / 1:1 CH_2Cl_2/[bmim][BF_4] (*B*)[b]	51	31	18 **49** [c]
5	MeOH (6 equiv) in $2.5 \cdot 10^{-3}$ N TsOH/[bmim][BF_4] (*B*)[b]	53	27	20 **47** [c]
6	10^{-2} N H_2SO_4 in 1:1 MeOH/[bzbim][BF_4] (*A*) [b]	84	-	16 **16** [c]

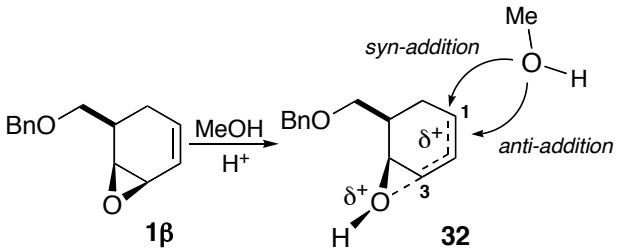
[a] See ref. 9a.

[b] (*A*): *protocol A*; (*B*): *protocol B* (see Tables 1 and 2 and ref. 10).

[c] Total amount of *1,4-addition products* (carbaglycosylating ability).

An examination of the regio- and stereoselectivity obtained in the methanolysis of epoxides **1α** and **1β**, limited to the more interesting *protocol B* reaction conditions (*B*, Tables 3 and 4), indicates how these new reaction conditions are able to increase the 1,4-regioselectivity in both the epoxides, particularly in epoxide **1β**. Actually, a 1.4 (from 57 to 80%, entries 2 and 4, Table 3) and 2.4 times increase (from 20 to 49% entries 1 and 4, Table 4) is observed in epoxide **1α** and **1β**, respectively.

In accordance with expectations, the presence of IL favors, by delocalization, an increase in partial positive charge at the C(1)-carbon further from the inductive electron- withdrawing effect of the protonated oxirane oxygen (structure **32**, Scheme 8 where only epoxide **1β** is shown for simplicity). Subsequent conjugate attack of the nucleophile (MeOH) on that carbon of epoxides **1α** and **1β** can more easily occur with the corresponding increased formation of *syn-* and *anti-1,4-addition products* (entries 4, Tables 3 and 4).[15]



Scheme 8. Effective delocalized intermediate species in the acid methanolysis of epoxide **1β** in the presence of IL.

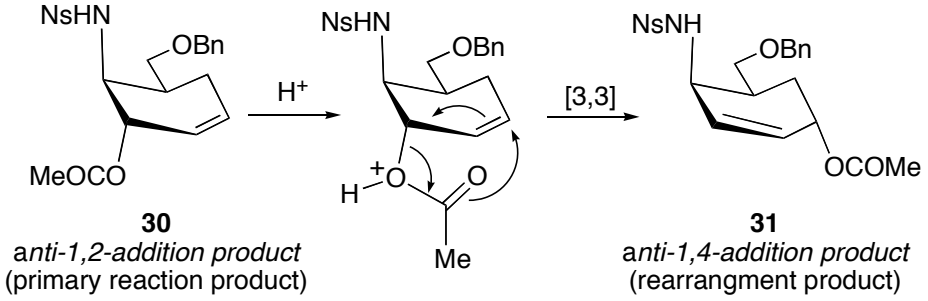
In both epoxides, the best result is obtained when the nucleophile is present only in a limited amount (6 equiv, *protocol B* reaction conditions) in a 1:1 CH_2Cl_2/IL mixture as the solvent in the presence of $2.5 \cdot 10^{-3}$ N TsOH as the acid (entries 4, Tables 3 and 4). Remarkably, the best result obtained with epoxide **1α** (80% 1,4-addition, entry 4, *protocol B*, Table 3) is accompanied, for the first time, with a consistent level of *syn*-stereoselectivity (76%, with *syn-*/*anti-1,4-addition product* ratio = 19:1).[15] The remaining is constituted by the usual *anti-1,2-addition product* which, in these conditions, reaches its lowest result (20%).

These last results confirm, once again, that epoxide **1α** is an efficient carbaglycosyl donor in the reaction with *O*-nucleophiles. At the same time, epoxide **1β** shows 1,4-addition values (49%, entry 4, *protocol B*, Table 4) which makes also this system interesting for further synthetic applications.

Differently from what observed with epoxides **1α** and **1β**, the use of ILs in the methanolysis of aziridines **9α-Ns** and **9β-Ns** was, unfortunately, unsuccessful and the regioselective results obtained under *protocol B* reaction conditions (entries 3, Tables 1 and 2) are completely similar to those previously obtained under the corresponding standard conditions (entries 2, Tables 1 and 2).

*2.3. Acid and basic acetolysis of aziridines **9α-Ns** and **9β-Ns***

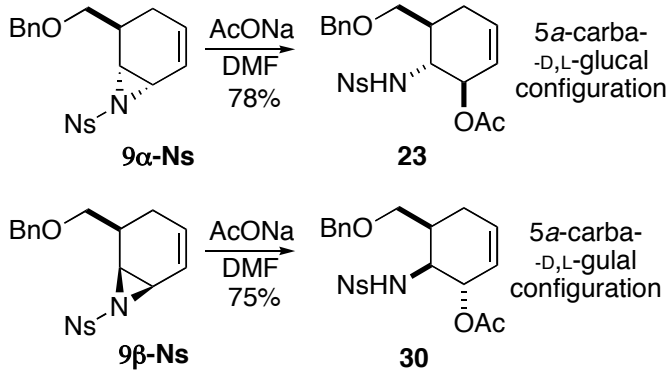
Acid acetolysis reactions, carried out both under *protocol A* and *B* reaction conditions, indicated that the regioselctive behavior of aziridines **9α-Ns** and **9β-Ns** is almost the same, giving similar mixtures of corresponding *1,2-* and *1,4-addition products* in both cases [about 30/40:70/60 *1,2-/1,4-addition products* ratio from **9α-Ns** (entries 4 and 5, Table 1) and **9β-Ns** (entries 4 and 5, Table 2)]. In this framework, it is worth noting that, in the case of azridine **9β-Ns**, *anti-1,4-adduct* **31** is the only *1,4-addition product* obtained and almost the same mixture of *anti-1,2-* **30** and *anti-1,4-adduct* **31** is obtained both under *protocol A* and *protocol B* reaction conditions. The peculiarity of this result with azridine **9β-Ns**, also in a comparison with the results obtained in the corresponding methanolysis reactions, let us think that *anti-1,4-adduct* **31** could not be an addition product, but the result of a partial isomerization of allyl acetate **30** (*anti-1,2-addition product*)**,** the only addition product and primary reaction product, in a type of acid-catalyzed suprafacial, completely stereoselective [3,3]sigmatropic rearrangement, as here shown (Scheme 9).[22]



Scheme 9. Hypothesized stereoselecive formation of *anti-1,4-addition product* **31** from corresponding *anti-1,2-addition product* **30** in the acid acetolysis of aziridine **9β-Ns**.

Alkaline acetolysis reactions [AcONa (4 equiv)/DMF*, protocol B*] of both aziridines **9α-Ns** and **9β-Ns** turned out to be completely 1,2-regio- and *anti*-stereoselective with the exclusive isolation of the corresponding *trans*-3-acetoxy-4-(*N*-nosylamino) derivative **23** and **30** from aziridine **9α-Ns** and **9β-Ns**, respectively (entries 6, Table 1 and 2, and Scheme 10). In this way, a simple, completely regio- and stereoselective procedure is available for the synthesis of 4-deoxy-4-

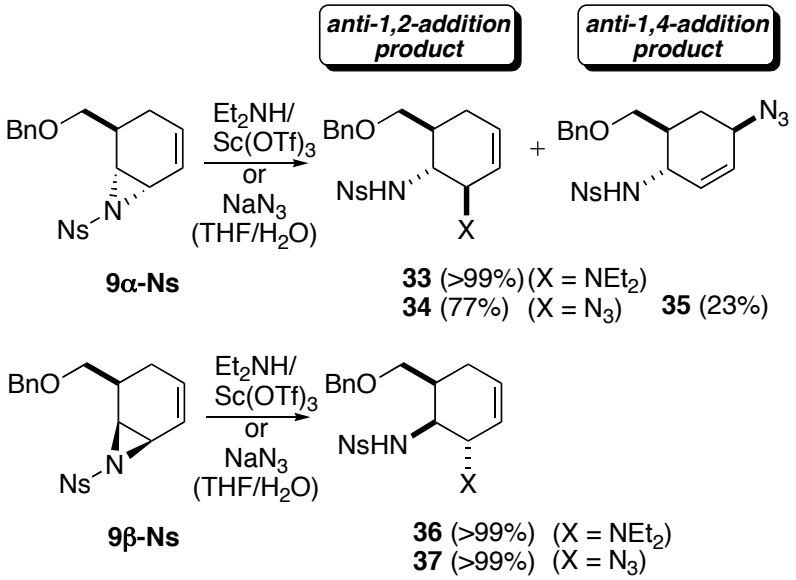
(*N*-nosylamino)-3-*O*-acetyl-derivatives having relative 5*a*-carba-D,L-glucal (**23**) and 5*a*-carba-D,L-gulal configuration (**30**), respectively, and containing easily removable *N*- and *O*-protective groups (Scheme 10).[8c]



Scheme 10. Alkaline acetolysis of aziridines **9α-Ns** and **9β-Ns**.

*2.4. Regio- and stereoselective behavior of N-nosyl aziridines **9α-Ns** and **9β-Ns** in nucleophilic addition reactions of N-Nucleophiles*

Aziridines **9α-Ns** and **9β-Ns** react with Et_2NH under *protocol A* reaction conditions (amine as the solvent) only in the presence of a Lewis acid, as $Sc(OTf)_3$. Under these conditions, both aziridines **9α-Ns** and **9β-Ns** afforded, in a completely 1,2-regio- and anti-stereoselective fashion, the corresponding *anti-1,2-addition product*, *trans*-3-(*N*,*N*-diethylamino)-4-(*N*-nosylamino) derivatives **33** and **36**, respectively (Scheme 11).



Scheme 11. Regio- and stereoselectivity of aminolysis and azidolysis of *N*-nosyl aziridines **9α-Ns** and **9β-Ns**.

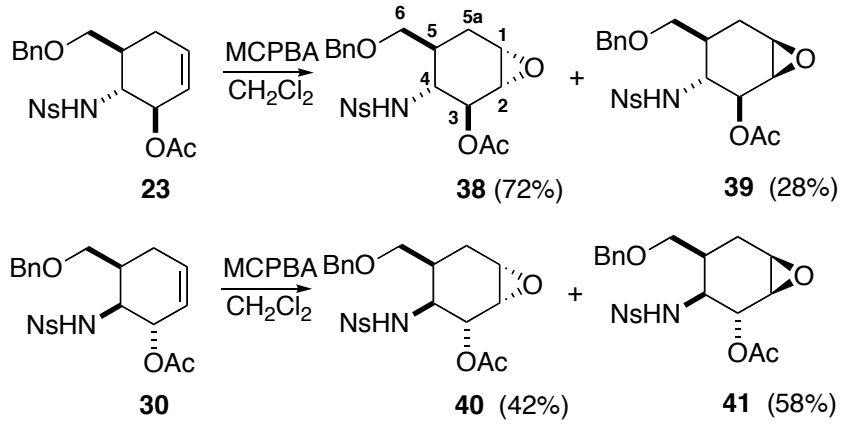
As for the azidolysis reactions, carried out by means of the previously described protocol (NaN_3 in THF/H_2O),[11] aziridine **9α-Ns** turned out to be mainly 1,2-regio- and anti-stereoselective, affording a 77:23 mixture of *anti-1,2-addition product*, *trans*-3-azido-4-(*N*-nosylamino) derivative **34** and *anti-1,4-addition product*, *trans*-1-azido-4-(*N*-nosylamino) derivative **35** (^1H NMR), whereas aziridine **9β-Ns** showed a completely anti-1,2-regioselective behavior with the isolation of *trans*-3-azido-4-(*N*-nosylamino) derivative **37**, as the only reaction product (Scheme 11).

The results obtained indicate that the behaviour of aziridines **9α-Ns** and **9β-Ns** with an amine and azide ion is dominated by the nucleophilicity of the reagents which directs, completely in **9β-Ns** (>99%) and mostly in **9α-Ns** (77-99%), the ring opening toward an anti-1,2-addition process.

*2.5. Functionalization of the double bond of model anti-1,2-addition products from N-nosyl aziridines **9α-Ns** and **9β-Ns***

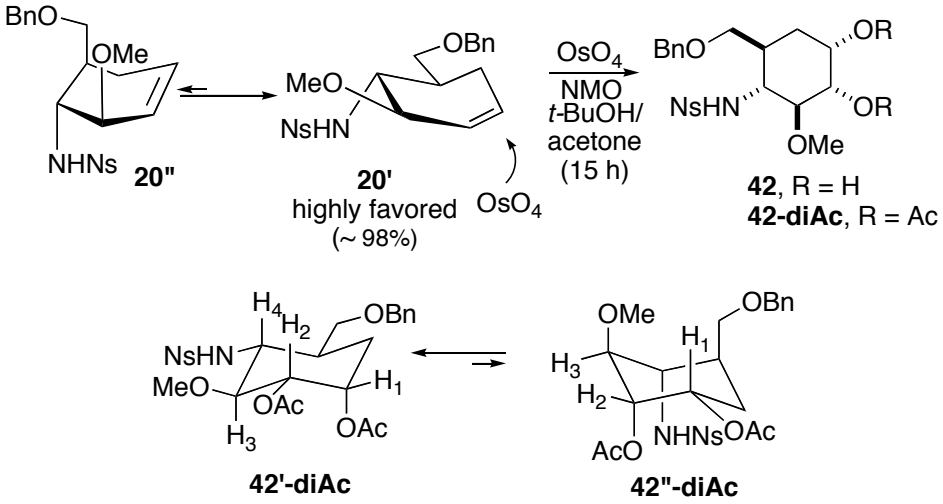
The reactivity in electrophilic reactions of the double bond of model *anti-1,2-addition products*, as *trans*-3-methoxy-4-(*N*-nosylamino) derivatives **20** and **27** and *trans*-3-acetoxy-4-(*N*-nosylamino) derivatives **23** and **30** obtained from aziridines **9α-Ns** and **9β-Ns**, respectively (Tables 1 and 2 and Scheme 10), was checked. These compounds were subjected to two typical electrophilic addition reactions such as epoxidation and catalytic dihydroxylation.

Epoxidation of *trans*-3-acetoxy-4-(*N*-nosylamino)-1,2-unsaturated derivatives **23** and **30** by the $MCPBA/CH_2Cl_2$ protocol is not stereoselective and mixtures of the corresponding diastereoisomeric epoxides **38** and **39** (72: 28 ratio), from **23,** and **40** and **41** (42:58 ratio), from **30**, were obtained, then separated by preparative TLC (Scheme 12) (see Supplementary data, sections 3.3 and 3.4, for NMR identifications of epoxides **38**-**41** and considerations on the absence of diastereoselectivity found in their formation).[23]



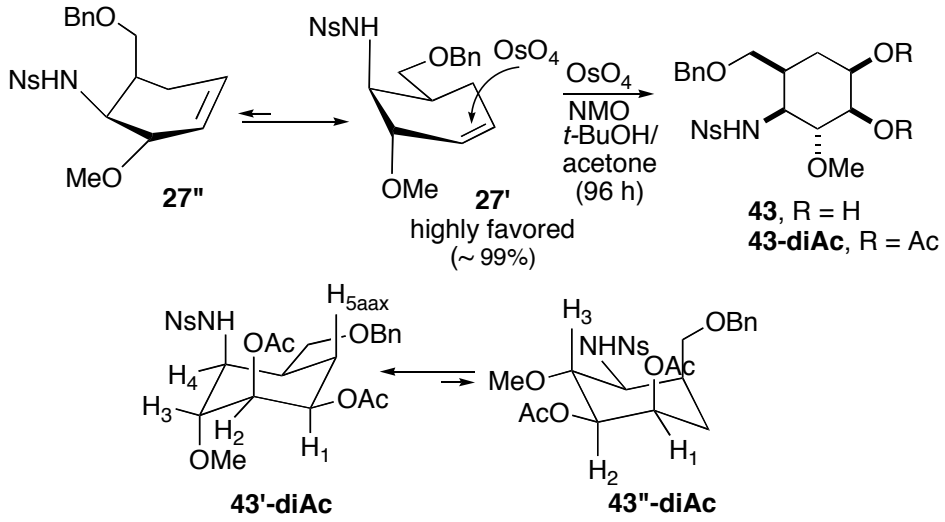
Scheme 12. Epoxidation by MCPBA/CH_2Cl_2 protocol of acetates **23** and **30** (*anti-1,2-addition products*).

On the contrary, catalytic dihydroxylation by OsO_4/NMO protocol of *trans*-3-methoxy-4-(*N*-nosylamino)-1,2-unsaturated derivatives **20** and **27**[24] carried out at room temperature in a *t*-BuOH/acetone mixture turned out to be completely stereoselective in both cases and *cis* diol **42**, a 4-deoxy-4-(*N*-nosylamino)-5*a*-carba-α-D,L-glucopyranose derivative, and **43**, a 4-deoxy-4-(*N*-nosylamino)-5*a*-carba-β-D,L-idopyranose derivative, were obtained from **20** and **27**, respectively, as the only reaction products (Schemes 13 and 14).



Scheme 13. Catalytic dihydroxylation of *anti-1,2-addition product* **20** by OsO_4/ NMO protocol.

In order to make the determination (^{1}H NMR) of the structure and configuration of the addition products easier, *cis* diols **42** and **43** were transformed into the corresponding diacetates **42-diAc** and **43-diAc** (Schemes 13 and 14).



Scheme 14. Catalytic dihydroxylation of *anti-1,2-addition product* **27** by OsO_4/ NMO protocol.

An accurate examination of the ^{1}H NMR spectra of these compounds, together with considerations based on the mechanism of the dihydroxylation reaction (complete *syn*-stereoselectivity) and an appropriate conformational analysis, confirmed the structure and configuration for **42-diAc** and **43-diAc**, and thus for the corresponding *cis* diols **42** and **43**, shown in Schemes 13 and 14.

In particular, the presence in the ^{1}H NMR spectrum of **42-diAc** of a trans diaxial relationship between the H(3) proton and the vicinal H(2) and H(4) protons ($J_{2,3} = J_{3,4} = 9.7$ Hz) unequivocally indicated the exclusive presence of the corresponding triequatorial conformer **42'-diAc**, the relative configuration at the C(1) and C(2) carbons and, as a consequence, the given structure (Scheme 13).

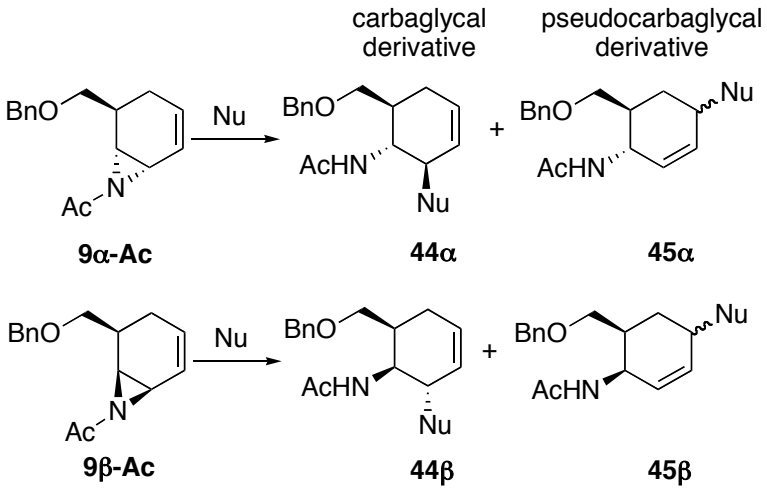
In the case of **43-diAc**, the presence in the corresponding ^{1}H NMR spectrum of a trans diaxial relationship between the H(1) proton and the axial H(5aax) proton ($J_{1,5aax} = 11.8$ Hz) and of an axial-equatorial relationship with the H(2) proton ($J_{1,2} = 3.1$ Hz) unequivocally indicated the exclusive presence of the corresponding conformer **43'-diAc** with the $-CH_2OBn$ side chain equatorial, the relative configuration at C(1) and C(2) carbons and, as a consequence, the given structure (Scheme 14).

The structures of **42-diAc** and **43-diAc** indicate that dihydroxylation occurred in both diastereoisomeric methoxy derivatives **20** and **27** with a completely *anti* facial selectivity with respect to the direction of the corresponding allyl substituent (-OMe). As for the remaining two substituents, while the $-CH_2OBn$ substituent seems to have no influence on the reaction, the β-directed –NHNs group, axial in conformer **27'**,[24] could be responsible for the observed longer reaction time (96 h) found for methoxy derivative **27,** when compared with diastereoisomeric

derivative **20** (15 h), by exerting steric hindrance to the β-face-approaching electrophile (Scheme 14).

*2.6. Synthesis of N-acetyl aziridines (3S,4R,5S)-**9α-Ac** and (3R,4S,5S)-**9β-Ac***

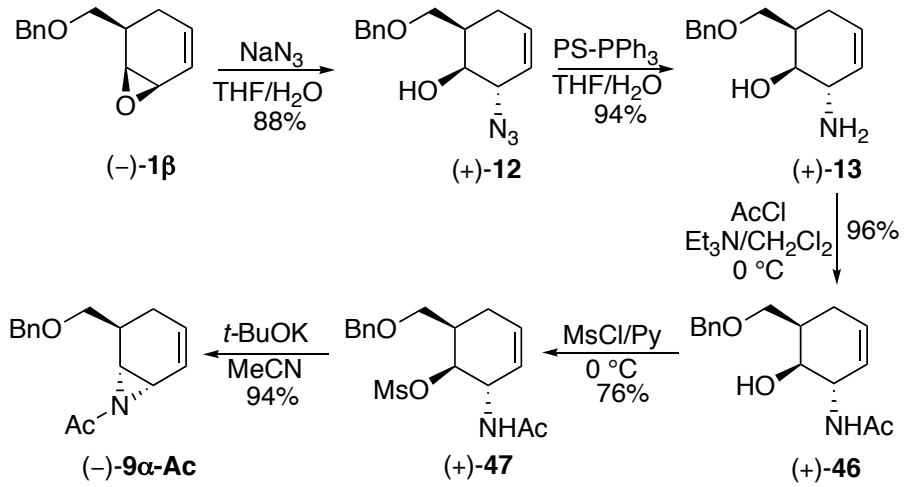
The interesting behavior observed with the racemic *N*-nosyl aziridines **9α-Ns** and **9β-Ns** in nucleophilic addition reactions, and the increased importance of aminocyclitols in medicinal chemistry[3-6] prompted us to synthesize structurally related enantiomerically pure aziridines. Considering that the –NHAc substituent is biologically interesting, we thought appropriate to direct our efforts toward enantiopure *N*-acetyl aziridines (3*S*,4*R*,5*S*)-**9α-Ac** and (3*R*,4*S*,5*S*)-**9β-Ac** (Scheme 15). Actually, in a consistent difference with aziridines **9α-Ns** and **9β-Ns** which transfer at the C(4)-carbon a –NHNs group (Scheme 2 and Tables 1 and 2), when aziridines **9α-Ac** and **9β-Ac** are subjected to the corresponding ring opening reactions, a -NHAc group is regio- and stereoselectively introduced at the C(4) carbon of an unsaturated carbasugar system [carbaglycal-**44α** and **44β** (*1,2-addition product*) and/or pseudocarbaglycal-derivative **45α** and **45β** (*1.4-addition product*)] with a clear added value to the products (Scheme 15). Both –NHAc and –NHNs[8c] group can be easily deprotected to corresponding free amino group. However, this step, probably unavoidable in –NHNs substituted derivatives in order to have biologically interesting compounds, could not be necessary in the case of corresponding –NHAc substituted products.



Scheme 15. Hypothesized behavior of aziridines **9α-Ac** and **9β-Ac** in nucleophilic addition reactions.

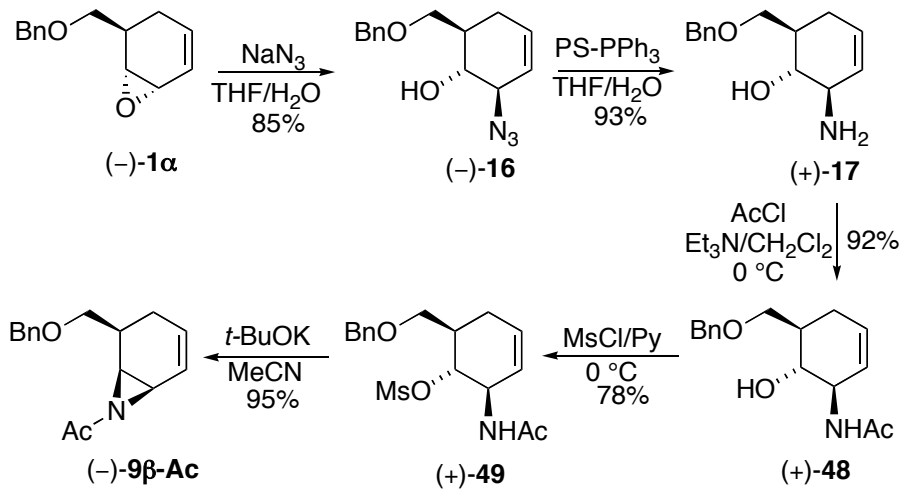
As previously described for the racemic *N*-nosyl aziridines **9α-Ns** and **9β-Ns** (Schemes 3 and 4), the synthesis of the new, non racemic *N*-acetyl aziridines **9α-Ac** and **9β-Ac** starts from the corresponding enantiomerically pure vinyl epoxide of opposite configuration (–)-**1β** and (–)-**1α**, respectively (Schemes 16 and 17).[9b]

Following the corresponding protocol, azidolysis (NaN_3/THF-H_2O) of epoxide (–)-**1β** afforded *trans* 3,4-azido alcohol (+)-**12**, as the only reaction product, which was then reduced by means of PS-PPh_3 to *trans* 3,4-amino alcohol (+)-**13**. The treatment of amino alcohol (+)-**13** by AcCl /NEt_3 in CH_2Cl_2 at 0°C turned out to be completely regioselective with the exclusive formation of the corresponding *N*-acetyl derivative (+)-**46** which was mesylated (MsCl/P) to give the fully protected derivative (+)-**47**. Base-catalyzed (*t*-BuOK) cyclization of *trans N*-acetyl-*O*-mesyl derivative (+)-**47** in anhydrous MeCN afforded the desired, enantiomerically pure *N*-acetyl aziridine (–)-**9α-Ac** [57% overall yield, for 5 steps starting from epoxide (–)-**1β**] (Scheme 16).



Scheme 16. Synthesis of vinyl *N*-acetyl aziridine (–)-**9α-Ac**.

The corresponding procedure starting from enatiomerically pure epoxide (–)-**1α**[9b] was followed for the synthesis of aziridine (–)-**9β-Ac**, as shown in Scheme 17. Azidolysis of epoxide (–)-**1α** by the NaN_3/1:1 THF/H_2O protocol afforded, as the only reaction product, *trans* 3,4-azido alcohol (–)-**16**, which was then reduced (PS-PPh_3 in THF/H_2O) to the corresponding *trans* 3,4-amino alcohol (+)-**17**. Regioselective *N*-acetylation of *trans* 3,4-amino alcohol (+)-**17** by AcCl/Et_3N in CH_2Cl_2 afforded *N*-acetyl derivative (+)-**48** which was mesylated (MsCl/Py) to give *trans N*-acetyl-*O*-mesyl derivative (+)-**49**. The treatment of (+)-**49** with *t*-BuOK in anhydrous MeCN afforded enantiomerically pure *N*-acetyl aziridine (–)-**9β-Ac** [54% overall yield for 5 steps starting from epoxide (–)-**1α**] (Scheme 17).



Scheme 17. Synthesis of vinyl *N*-acetyl aziridine (–)-**9β-Ac**.

As the chiral starting epoxides (–)-**1α** and (–)-**1β** had been prepared in a stereodivergent fashion starting from commercially available (+)-tri-*O*-acetyl-D-glucal, the common starting material and chiral source,[9b] the same can be said for enantiomerically pure *N*-acetyl aziridines (–)-**9α-Ac** and (–)-**9β-Ac** which derive from epoxides (–)-**1β** and (–)-**1α**, respectively, in a completely stereoselective fashion.

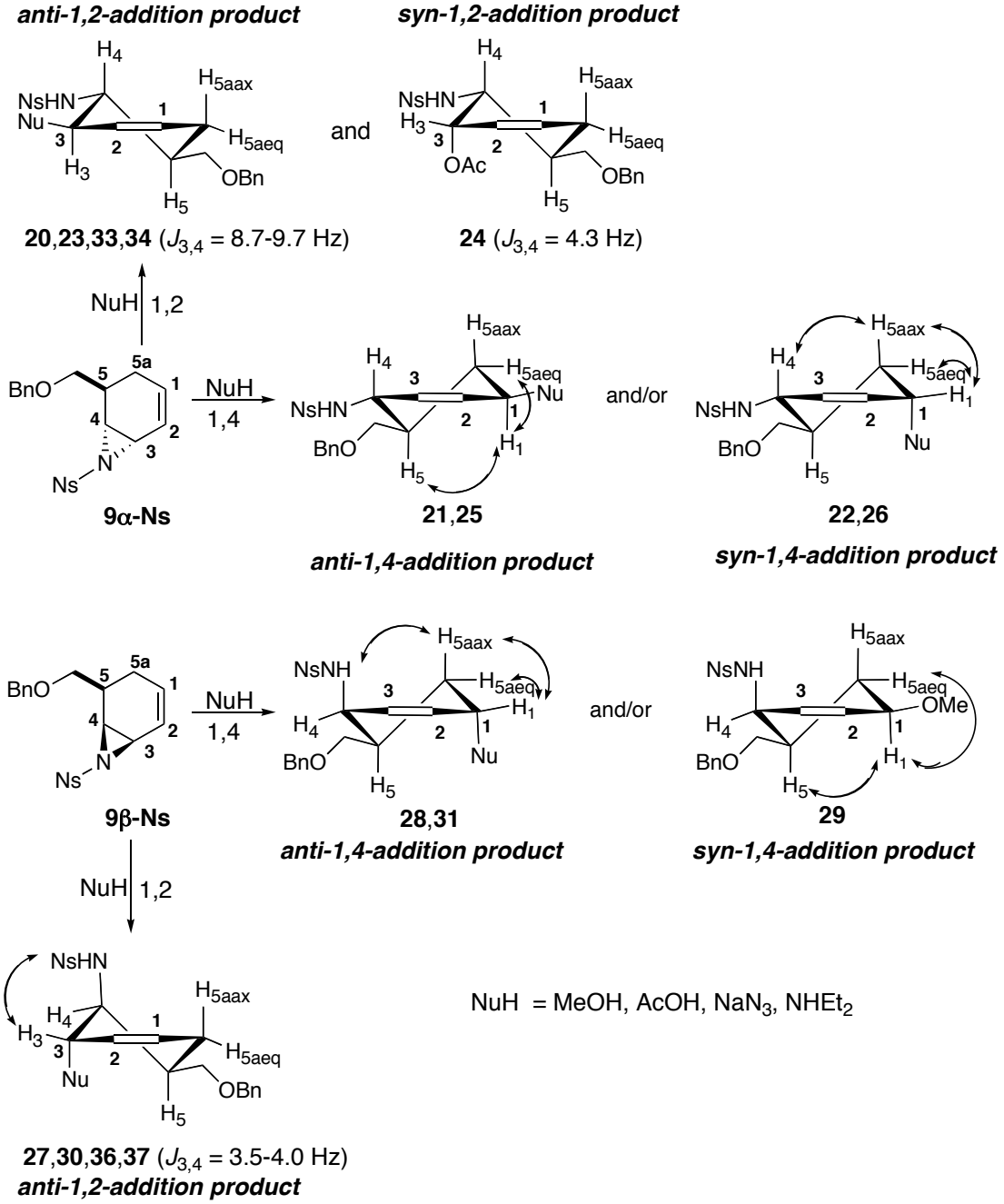
Contrary to expectations based on racemic *N*-nosyl aziridines **9α-Ns** and **9β-Ns**, the corresponding enantiomerically pure *N*-acetyl aziridines (–)-**9α-Ac** and (–)-**9β-Ac** turned out to be not particularly stable and had to be stored at –20 °C.

2.7. Structures and configurations

The structure and configuration of regioisomeric *1,2-* and *1,4-addition products* obtained in the opening reactions of aziridines **9α-Ns** and **9β-Ns** have been determined by compared analysis of homonuclear scalar (COSY), dipolar (NOESY) and heteronuclear scalar (HSQC) correlations in their 2D NMR maps and by taking into account that the configuration at the C(4)-carbon necessarily corresponds to that of the starting aziridine.

1,2-Addition products obtained in the opening reactions of aziridines **9α-Ns** and **9β-Ns** have been characterized by the presence of scalar correlations of the corresponding vinyl H(1) proton with the methylene protons at the C(5a)-carbon.

The relative configuration at the C(3)-carbon of *anti-1,2-addition products* **20**, **23**, **33** and **34**, obtained from aziridine **9α-Ns,** and **27**, **30**, **36** and **37**, obtained from aziridine **9β-Ns,** has been determined by the coupling constant value between the diaxial ($J_{3,4}$ = 8.7-9.7 Hz) or diequatorial H(3)-H(4) proton relationship ($J_{3,4}$ = 3.5-4.0 Hz) in the corresponding compounds from **9α-Ns** and **9β-Ns**, respectively, and by the presence of NOE between the H(3) proton and the NH in the corresponding compounds from aziridine **9β-Ns**. Moreover, a theoretical conformational study had indicated that *anti-1,2-addition products* from both aziridines **9α-Ns** and **9β-Ns** almost completely exist in the corresponding conformer with the $-CH_2OBn$ side chain equatorial (Scheme 18).[24] In this framework, the presence of a diequatorial H(3)-H(4) protons relationship ($J_{3,4}$ = 4.3 Hz) in compound **24**, obtained in the acetolysis of aziridine **9α-Ns**, clearly indicated the corresponding relative configuration at the C(3)-carbon and, as a consequence, the structure of *syn-1,2-addition product* (Scheme 18).[17]



Scheme 18. H(3)-H(4) protons coupling constant ($J_{3,4}$) in *anti-1,2-addition products* from aziridines **9α-Ns** and **9α-Ns** and *syn-1,2-addition product* from aziridine **9α-Ns**, NOEs in *anti-1,2-addition products* from aziridine **9β-Ns** and *syn-* and *anti-1,4-addition products* from both aziridines **9α-Ns** and **9β-Ns**.

1,4-Addition products obtained in the opening reactions of aziridines **9α-Ns** and **9β-Ns** have been characterized by means of the corresponding allyl H(1) proton which gives rise to intense NOEs on the methylene ring protons [H($5a_{ax}$) and H($5a_{eq}$)] and on the H(2) vinyl proton (Scheme 18).

The relative configuration at the C(1)-carbon of *anti-1,4-addition products* **21** and **25** from aziridine **9α-Ns** has been established on the basis of the intense H(1)/H(5) dipolar interaction, as expected for a H(1)/H(5) *cis*-1,3-diaxial arrangement. By contrast, in the case of the corresponding *syn-1,4-addition products* **22** and **26**, both H(1) and H(4) protons produce NOE on the methylene proton H($5a_{ax}$), confirming the presence of a cis relationship between the H(1) and H(4) protons.

In accordance with the above described results and with the structures shown in Scheme 18, opposite contacts are observed in the case of *1,4-addition products* obtained by nucleophilic addition to aziridine **9β-Ns**: an intense H(1)/H(5) dipolar interaction is found in *syn-1,4-addition product* **29**, whereas in the corresponding *anti-1,4-addition products* **28** and **31**, H(1) and NH protons produce NOE on the methylene proton H($5a_{ax}$).

In the case of epoxides **36-41** (Scheme 12), due to the conformational strain of the bicyclo structures, the relative configurations at the C(1) and C(2) carbons have been established on the basis of the comparison of dipolar interactions produced by H(1), H(4) or NH on the methylene ring protons H($5a_{ax}$)/H($5a_{eq}$) (Scheme 12) in a similar way as discussed for the assignment of the configuration at the C(1) carbon of *syn-1,4-addition products* from aziridine **9α-Ns** (epoxides **38** and **40**) or *anti-1,4-addition products* from aziridine **9β-Ns** (epoxides **39** and **41**) (see Supplementary data, section 3.3).

2.8. Conclusions

The new carba-D,L-allal- and carba-D,L-galactal-derived vinyl *N*-nosyl aziridines **9α-Ns** and **9β-Ns** have been prepared and their regio- and stereoselective behavior examined in ring opening reactions with *O*- (MeOH and AcOH) and *N*-nucleophiles (azide anion and diethylamine). In particular, by means of acid methanolysis, taken as a model reaction, their tendency to give *1,4-addition products* (the so-called carbaglycosylating ability, as the total amount of *syn*- and/or *anti-1,4-adducts*) was checked, in view of a possible use of these activated carbaglycal system in the regio- and stereoselective construction of alkyl 4-deoxy-4-(*N*-nosylamino)-2,3-unsaturated-5*a*-carba-*O*-glycosides. The results have indicated that the carboglycosylating ability of aziridines **9α-Ns** and **9β-Ns** is similar (62%, entry 1 Table 1, and 60%, entry 2 Table 2, respectively) to that of the corresponding carba-D,L-allal-derived epoxide **1α** (57-68%), and decidedly superior to carba-D,L-galactal epoxide **1β** (20%) (Scheme 1).[9a] The use of an Ionic Liquid (IL), as co-solvent in the acid methanolysis reaction, determines a consistent increase in the carboglycosylating ability of epoxides **1α** (80%) and **1β** (49%) (entries 4, Tables 3 and 4), but has no effect with aziridines **9α-Ns** and **9β-Ns**. The catalytic dihydroxylation by OsO_4/NMO of the residual C(1)-C(2) unsaturation

of model *anti-1,2-addition products* from aziridines **9α-Ns** and **9β-Ns** turned out to be completely stereoselective and could constitute a new protocol for the stereoselective synthesis of 4-*N*-protected-aminocyclitol-derivatives. Alternatively, MCPBA oxidation of further model *anti-1,2-addition products* led to pairs of diastereoisomeric epoxides which were obtained pure by TLC separation. These epoxides could act as effective and stereoselective carbaglycosyl donors for the synthesis of 4-deoxy-4-(*N*-nosylamino)-5*a*-carba-D,L-α- or -β-glycosides,[23] and appropriate studies will be reported in due course on the regio- and stereoselective behavior of these oxirane systems in the corresponding nucleophilic opening reactions in order to evaluate this point.

3. Experimental

3.1.General

All reactions were performed in a flame-dried modified Schlenk (Kjeldahl shape) flask fitted with a glass stopper or rubber septum under a positive pressure of argon. Flash column chromatography was performed employing 230-400 mesh silica gel (Macherey-Nagel). Analytical TLC were performed on Alugram SIL G/UV_{254} silica gel sheets (Macherey-Nagel) with detection by 0.5% phosphomolybdic acid solution in 95% EtOH. NaN_3, PS-PPh_3, NsCl, MsCl, AcOH, HPLC grade MeOH, anhydrous CH_2Cl_2 and MeCN, pyridine and DMF over molecular sieves were purchased from Aldrich and used without purification. Et_2O and THF were distilled from sodium/benzophenone. Racemic epoxides **1α** and **1β**,[9a] and enantiomerically pure epoxides (–)-**1α** and (–)-**1β**,[9b] were prepared as previously described. Racemic *trans* 3,4-azido alcohols **12** and **16** had been previously described.[9a] Routine ^1H and ^{13}C NMR spectra were recorded at 250 and 62.5 MHz, respectively. ^1H NMR COSY, NOESY and HSQC experiments were performed with a spectrometer operating at 600 MHz. IR spectra were obtained by means of a FTIR spectrophotometer. Elemental analyses were performed at Dipartimento di Farmacia, University of Pisa, by means of Carlo Erba Automated CHN Analyzer model 1106.

*3.2. Synthesis of N-nosyl aziridine **9α-Ns***

*3.2.1. Azidolysis of epoxide **1β** by NaN_3 in 1:1 THF/H_2O*

A solution of epoxide **1β** (0.150 g, 0.694 mmol) in distilled THF (1.70 mL) was added to a solution of NaN_3 (0.068 g, 1.041 mmol, 1.5 equiv) in H_2O (1.70 mL) and the reaction mixture was stirred for 20 h at room temperature. After dilution with Et_2O, evaporation of the washed (brine) organic solution gave *trans* 3,4-azido alcohol **12** (0.155 g, 86% yield),[9a] pure as a yellow liquid, which was used in the next step without any further purification.

*3.2.2. 6-O-Benzyl-3-deoxy-3-amino-5a-carba-D,L-gulal (**13**)*

Polymer-supported PPh_3 (PS-PPh_3, 3 mmol/g) (0.339 g, 1.017 mmol, 1.70 equiv) was washed with CH_2Cl_2, acetone and methanol, dried at 60°C for 3 h and allowed to swell in THF/H_2O 20:1 (6.0 mL) for 30 minutes without stirring.[8b] A solution of *trans* 3,4-azido alcohol **12**[9a] (0.155 g, 0.598 mmol) in THF (1.0 mL) was added dropwise to the above prepared suspension of PS-PPh_3 in THF/H_2O and the reaction mixture was stirred for 48 h at room temperature. Dilution with Et_2O and evaporation of the filtered (Celite®) organic solution afforded a crude product consisting of

trans 3,4-amino alcohol **13** (0.134 g, 96% yield), practically pure as a white, crystalline solid, mp 96-98°C; R_f= 0.15 (9:1 AcOEt/MeOH); FTIR ν_{max} (Nujol) 3355 (broad), 1453, 1364, 1199, 1176, 1073, 909 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.27-7.40 (m, 5H), 5.69 (ddt, 1H, *J* = 9.9, 3.3, 1.3 Hz), 5.54-5.63 (m, 1H), 4.52 (s, 2H), 3.73 (dd, 1H, *J* = 6.7, 2.2 Hz), 3.66 (dd, 1H, *J* = 6.7, 2.9 Hz), 3.59 (dd, 1H, *J* = 9.2, 5.4 Hz), 3.22-3.29 (m, 1H), 2.20-2.35 (m, 1H), 2.05-2.15 (m, 2H), 1.90-2.05 (m, 2H). ^{13}C NMR (CD_3OD) δ 137.9, 129.7, 128.6, 128.0, 127.8, 127.2, 76.1, 73.7, 72.6, 52.0, 35.2, 26.2. Anal. Calcd. for $C_{14}H_{19}NO_2$: C 72.70; H, 8.20; N, 6.00. Found: C, 72.55; H, 8.01; N, 5.74.

*3.2.3. 6-O-Benzyl-3-deoxy-3-(N-nosylamino)-5a-carba-D,L-gulal (**14**)*

A solution of *trans* 3,4-amino alcohol **13** (0.134 g, 0.575 mmol) in anhydrous CH_2Cl_2 (4.5 mL) was treated at 0°C with Et_3N (0.096 mL, 0.69 mmol, 1.2 equiv) and NsCl (0.140 g, 0.632 mmol, 1.1 equiv) and the reaction mixture was stirred for 2 h at room temperature. Dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude residue consisting of *N*-nosyl derivative **14** (0.238 g, 99% yield), as a yellow viscous liquid, sufficiently pure to be directly used in the next step: R_f= 0.42 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3310, 1539, 1416, 1365, 1248, 1070, 788 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.09-8.18 (m, 1H), 7.57-7.72 (m, 3H), 7.27-7.37 (m, 5H), 5.78-5.90 (m, 1H), 5.28-5.39 (m, 2H), 4.44 (s, 2H), 4.31-4.39 (m, 1H), 3.52-3.64 (m, 1H), 3.20-3.40 (m, 3H), 1.84-2.36 (m, 2H), 1.46-1.77 (m, 1H). ^{13}C NMR (CD_3Cl) δ 147.4, 137.7, 133.8, 133.6, 132.8, 131.3, 130.6, 128.2, 127.5, 127.4, 125.0, 122.6, 73.1, 71.9, 71.1, 54.2, 45.9, 33.9, 24.2. Anal. Calcd. for $C_{20}H_{22}N_2O_6S$: C 57.41; H, 5.30; N, 6.69. Found: C, 57.26; H, 5.11; N, 6.43.

*3.2.4. 6-O-Benzyl-4-O-mesyl-3-deoxy-3-(N-nosylamino)-5a-carba-D,L-gulal (**15**)*

A solution of *N*-nosyl derivative **14** (0.458 g, 1.096 mmol) in anhydrous pyridine (5.0 mL) was treated at 0°C with MsCl (0.169 mL, 2.192 mmol, 2.0 equiv) and the reaction mixture was stirred for 12 h at the same temperature. Dilution with CH_2Cl_2 and evaporation of the washed (10% aqueous HCl, saturated aqueous $NaHCO_3$ and brine) organic layer afforded a crude residue (0.525 g) consisting of *trans N*-nosyl-*O*-mesyl derivative **15** (H^1 NMR) which was subjected to flash chromatography. Elution with a 1:1 hexane/ AcOEt mixture afforded *trans N*-nosyl-*O*-mesyl derivative **15** (0.478 g, 88% yield), pure as a white solid mp 53-55 °C : R_f = 0.33 (1:1 hexane/AcOEt); FTIR ν_{max}(Nujol) 3310, 1537, 1414, 1344, 1165, 1072, 918, 844, 731 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.22-8.31 (m, 1H), 7.65-7.73 (m, 2H), 7.58-7.64 (m, 1H), 7.30-7.43 (m, 5H), 5.95-6-05 (m, 1H), 5.42-5.52 (m, 1H), 5.35 (d, 1H, *J* = 6.8 Hz), 4.91-4.98 (m, 1H), 4.42 (d, 1H, *J* = 11.6 Hz), 4.37 (d, 1H, *J* = 11.6 Hz), 4.22 (bs, 1H), 3.36-3-47 (m, 2H), 2.97 (s, 3H), 2.27-2.42 (m, 1H),

1.98-2.15 (m, 1H), 1.79-1.97 (m, 1H). ^{13}C NMR (CD_3Cl) δ 147.9, 137.9, 134.0, 133.3, 132.6, 132.1, 128.7, 128.2, 128.1, 125.6, 121.4, 77.4, 73.3, 69.4, 52.4, 37.8, 32.8, 23.5. Anal. Calcd. for $C_{21}H_{24}N_2O_8S_2$: C 50.79; H, 4.87; N, 5.63. Found: C, 50.48; H, 4.61; N, 5.59.

3.2.5 (1S, 5S*,6R*)-5-(Benzyloxymethyl)-7-nosyl-7-azabicyclo[4.1.0]hept-2-ene (**9α-Ns**)*

A solution of *trans N*-nosyl-*O*-mesyl derivative **15** (0.145 g, 0.292 mmol) in anhydrous MeCN (15.0 mL) was treated with K_2CO_3 (0.121 g, 0.877 mmol, 3.0 equiv) at room temperature and the reaction mixture was stirred for 1 h at the same temperature. After dilution with Et_2O, evaporation of the filtered organic solution afforded *N*-nosyl aziridine **9α-Ns** (0.113 g, 97% yield) practically pure, as a pale yellow liquid: R_f = 0.60 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 1542, 1364, 1332, 1164, 1123, 1087, 1058, 950 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.17-8.27 (m, 1H), 7.67-7-79 (m, 3H), 7.28-7.41 (m, 5H), 5.88-5.99 (m, 1H), 5.78-5.87 (m, 1H), 4.52 (s, 2H), 3.56-3-64 (m, 1H), 3.28-3.48 (m, 3H), 2.10-2.26 (m, 2H), 1.94-2.09 (m, 1H). ^{13}C NMR (CD_3Cl) δ 147.8, 134.3, 132.4, 131.2, 128.6, 127.8, 124.7, 124.9, 124.0, 121.1, 73.3, 70.5, 44.9, 38.9, 29.9, 23.7. Anal. Calcd. for $C_{20}H_{20}N_2O_5S$: C 59.99; H, 5.03; N, 6.99. Found: C, 59.87; H, 4.84; N, 6.71.

*3.3. Synthesis of N-nosyl aziridine **9β-Ns***

*3.3.1. Azidolysis of epoxide **1α** by NaN_3 in 1:1 THF/H_2O*

A solution of epoxide **1α** (0.138 g, 0.639 mmol) in distilled THF (1.6 mL) was added to a solution of NaN_3 (0.062 g, 0.958 mmol, 1.5 equiv) in H_2O (1.6 mL) and the reaction was stirred for 20 h at room temperature. After dilution with Et_2O, evaporation of the washed (brine) organic solution afforded *trans* 3,4-azido alcohol **16** (0.136 g, 82% yield),[9a] pure as a yellow liquid, which was used in the next step without any further purification.

*3.3.2. 6-O-Benzyl-3-deoxy-3-amino-5a-carba-D,L-glucal (**17**)*

PS-PPh_3 (3 mmol/1 g) (0.617 g, 1.85 mmol, 1.70 equiv) was washed with CH_2Cl_2, acetone and methanol, dried at 60°C for 3 h and allowed to swell in THF/H_2O 20:1 (10.5 mL) for 30 minutes without stirring.[8b] A solution of *trans* 3,4-azido alcohol **16**[9b] (0.282 g, 1.088 mmol) in THF (2.0 mL) was added dropwise to the above suspension of PS-PPh_3 in THF/H_2O and the reaction mixture was stirred for 48 h at room temperature. Dilution with Et_2O and evaporation of the filtered (Celite®) organic solution afforded a crude product consisting of *trans* 3,4-amino alcohol **17** (0.241 g, 95% yield), practically pure as a white solid, mp 92-95 °C: R_f = 0.10 (9:1 AcOEt/MeOH); FTIR ν_{max}(Nujol) 3350 (broad), 1455, 1364, 1192 1176, 1084, 915 cm^{-1}. ^{1}H NMR [$(CD_3)_2CO$] δ 7.20-7.39 (m, 5H), 5.66 (ddd, 1H, *J* = 9.5, 4.1, 1.7 Hz), 5.13 (ddd, 1H, *J* = 9.5, 4.5, 2.6 Hz), 4.51 (s, 2H),

3.87-3.95 (m, 1H), 3.76 (dd, 1H, *J* = 9.2, 3.7 Hz), 3.65-3.72 (m, 1H), 3.60 (dd, 1H, *J* = 9.2, 6.2 Hz), 2.65-3.00 (m, 3H), 2.26-2.37 (m, 1H), 2.07-2.17 (m, 1H), 1.81-1.93 (m, 1H). ^{13}C NMR (CD_3OD) δ 139.9, 129.5, 129.3, 128.7, 128.6, 128.4, 76.4, 74.3, 72.5, 56.7, 41.4, 30.4. Anal. Calcd. for $C_{14}H_{19}NO_2$: C 72.70; H, 8.20; N, 6.00. Found: C, 72.55; H, 7.91; N, 5.66.

*3.3.3. 6-O-Benzyl-3-deoxy-3-(N-nosylamino)-5a-carba-D,L-glucal (**18**)*

A solution of *trans* 3,4-amino alcohol **17** (0.230 g, 0.987 mmol) in anhydrous CH_2Cl_2 (8.0 mL) was treated at 0°C, with Et_3N (0.165 mL, 1.184 mmol, 1.2 equiv) and NsCl (0.240 g, 1.084 mmol, 1.1 equiv) and the reaction mixture was stirred for 4 h at room temperature. Dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude residue consisting of *N*-nosyl derivative **18** (0.408 g, 99% yield), as a yellow viscous liquid, sufficiently pure to be directly used in the next step: R_f= 0.24 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3357 (broad), 1537, 1439, 1164, 1118, 1070, 1023, 736. cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.13-8.20 (m, 1H), 7.87-7.93 (m, 1H), 7.68-7.74 (m, 2H), 7.27-7.37 (m, 5H), 5.68 (ddd, 1H, *J* = 10.0, 4.6, 2.3 Hz), 5.58 (d, 1H, *J* = 7.8 Hz), 5.38-5.46 (m, 1H), 4.50 (d, 1H, *J* = 12.0 Hz), 4.45 (d, 1H, *J* = 12.0 Hz), 3.86-3.98 (m, 1H), 3.59 (dd, 1H, *J* = 9.3, 4.2 Hz), 3.52 (dd, 1H, *J* = 9.3, 6.1 Hz), 3.47-3.59 (m, 1H), 3.31-3.35 (m, 1H), 1.82-2.14 (m, 3H). ^{13}C NMR (CD_3Cl) δ 148.0, 137.8, 133.5, 133.1, 131.5, 129.1, 128.7, 128.1, 127.9, 126.3, 125.6, 74.5, 73.6, 72.7, 59.6, 39.6, 28.0. Anal. Calcd. for $C_{20}H_{22}N_2O_6S$: C 57.41; H, 5.30; N, 6.69. Found: C, 57.18; H, 5.06; N, 6.35.

*3.3.4. 6-O-Benzyl-4-O-mesyl-3-deoxy-3-(N-nosylamino)-5a-carba-D,L-glucal (**19**)*

A solution of *N*-nosyl derivative **18** (0.458 g, 1.096 mmol) anhydrous pyridine (5.0 mL) was treated at 0°C with MsCl (0.169 mL, 2.192 mmol, 2.0 equiv) and the reaction mixture was stirred for 12 h at the same temperature. Dilution with CH_2Cl_2 and evaporation of the washed (10% aqueous HCl, saturated aqueous $NaHCO_3$ and brine) organic layer afforded a crude residue (0.525 g) consisting of *trans* *N*-nosylamino–*O*-mesyl derivative **19** (H^1 NMR) which was subjected to flash chromatography. Elution with a 1:1 hexane/ AcOEt mixture afforded *trans* *N*-nosyl–*O*-mesyl derivative **19** (0.478 g, 88% yield), pure as a white solid, mp 53-55 °C: R_f = 0.22 (1:1 hexane/AcOEt); FTIR ν_{max}(Nujol) 3325, 1539, 1441, 1423, 1344, 1167, 1119, 1094, 952, 776 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.11-8.19 (m, 1H), 7.87-7.93 (m, 1H), 7.73-7.81 (m, 2H), 7.28-7.37 (m, 5H), 5.79 (d, 1H, *J* = 9.6 Hz), 5.65-5.75 (m, 1H), 4.99 (ddd, 1H, *J* = 10.1, 4.0, 2.3 Hz), 4.82 (dd, 1H, *J* = 9.4, 8.4 Hz), 4.61 (d, 1H, *J* = 11.5 Hz), 4.45 (d, 1H, *J* = 11.5 Hz), 4.26-4.39 (m, 1H), 3.66 (dd, 1H, *J* = 9.4, 4.5 Hz), 3.58 (dd, 1H, *J* = 9.4, 2.7 Hz), 3.22 (s, 3H), 2.15-2.41 (m, 3H). ^{13}C NMR (CD_3Cl) δ 148.3, 138.2, 134.1, 133.4, 130.9, 130.8, 130.7, 128.5, 128.1, 127.8, 125.7, 123.9, 81.1, 73.4, 69.5,

56.7, 52.7, 39.7, 29.9. Anal. Calcd. for $C_{21}H_{24}N_2O_8S_2$: C 50.79; H, 4.87; N, 5.63. Found: C, 50.71; H, 4.92; N, 5.54.

3.3.5. (1R, 5S*,6S*)-5-(Benzyloxymethyl-)7-nosyl-7-azabicyclo[4.1.0]hept-2-ene* ***(9β-Ns)***

A solution of *trans N*-nosyl-*O*-mesyl derivative **19** (0.227 g, 0.458 mmol) in anhydrous MeCN (22.0 mL) was treated with K_2CO_3 (0.190 g, 1.374 mmol, 3.0 equiv) at room temperature, and the reaction mixture was stirred for 1 h at the same temperature. After dilution with Et_2O, evaporation of the filtered organic solution afforded *N*-nosyl aziridine **9β-Ns** (0.175 g, 95% yield) practically pure, as a pale yellow liquid: R_f = 0.58 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 1541, 1364, 1331, 1161, 1123, 1089, 1059, 948 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.10-8.19 (m, 1H), 7.59-7-78 (m, 3H), 7.28-7.38 (m, 5H), 5.85-6.04 (m, 2H), 4.49 (d, 1H, *J* = 11.8 Hz), 4.41 (d, 1H, *J* = 11.8 Hz), 3.59 (dt, 1H, *J* = 7.1, 1.8 Hz), 3.42-3.56 (m, 3H), 2.02-2.19 (m, 2H), 1.94-2.09 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 148.3, 138.4, 134.3, 133.6, 132.1, 131.1, 128.6, 127.8, 124.7, 120.4, 73.5, 73.1, 44.5, 40.1, 31.5, 24.3. Anal. Calcd. for $C_{20}H_{20}N_2O_5S$: C 59.99; H, 5.03; N, 6.99. Found: C, 59.75; H, 4.92; N, 6.68. CONTROLLARE SPETTRO

3.4. Reactions of N-nosyl aziridines ***9α-Ns*** *and* ***9β-Ns*** *with MeOH (O-nucleophile) under acid conditions*

3.4.1. Methanolysis of N-nosyl aziridine ***9α-Ns*** *with 0.2 N H_2SO_4/MeOH (protocol A)*

N-Nosyl aziridine **9α-Ns** (0.060 g, 0.15 mmol) was added to 0.2 N H_2SO_4/MeOH (6.0 mL) and the resulting reaction mixture was stirred 2 h at room temperature. After dilution with CH_2Cl_2, solid $NaHCO_3$ was added. Evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution, afforded a crude product (0.062 g, 96% yield) consisting of a 38:30:32 mixture of (*N*-nosylamino)-methoxy derivatives **20**, **21** and **22** (^1H NMR) (entry 1, Table 1) which was subjected to preparative TLC, using a 9:1 CH_2Cl_2/(*i*-Pr)$_2O$ mixture as the eluant. Extraction of the three most intense bands afforded *trans*-3-methoxy-4-(*N*-nosylamino)- **20** (0.013 g, 20% yield), *trans*- **21** (0.012 g, 19% yield) and *cis*-1-methoxy-4-(*N*-nosylamino) derivative **22** (0.012 g, 18% yield).

6-O-Benzyl-3-O-methyl-4-deoxy-4-(N-nosylamino)-5a-carba-D,L-glucal (**20**): a liquid, R_f= 0.31 (6:4 hexane/AcOEt); FTIR ν_{max}(liquid film) 3346, 1536, 1441, 1341, 1162, 1086, 732 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.10-8.18 (m, 1H), 7.83-7.91 (m, 1H), 7.62-7.75 (m, 2H), 7.28-7.40 (m, 5H), 5.72-5.84

(m, 1H), 5.58 (d, 1H, *J* = 10.0 Hz), 5.47 (d, 1H, *J* = 8.2 Hz), 4.56 (d, 1H, *J* = 11.7 Hz), 4.50 (d, 1H, *J* = 11.7 Hz), 3.80 (dd, 1H, *J* = 9.1, 4.4 Hz), 3.51-3.60 (m, 3H), 2.72 (s, 3H), 2.26-2.46 (m, 1H), 1.94-2.19 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 146.6, 137.5, 135.2, 131.9, 131.8, 130.3, 128.0, 127.5, 127.0, 126.8, 124.0, 123.6, 80.4, 72.5, 70.7, 56.8, 54.6, 37.9, 28.5. Anal. Calcd. for $C_{21}H_{24}N_2O_6S$: C 58.32; H, 5.59; N, 6.47. Found: C, 58.44; H, 5.31; N, 6.14.

Methyl 6-O-benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-β-D,L-erithro-hex-2-enopyranoside (**21**): a liquid, R_f= 0.39 [9:1 CH_2Cl_2/(*i*-Pr)$_2$O]; FTIR ν_{max}(liquid film) 3390, 1537, 1452, 1416, 1344, 1161, 1077, 1061, 1010 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.10 (dd, 1H, *J* = 7.4, 2.0 Hz), 7.84 (dd, 1H, *J* = 7.4, 1.8 Hz), 7.60-7.74 (m, 2H), 7.26-7.41 (m, 5H), 5.78 (ddd, 1H, *J* = 10.1, 3.7, 1.8 Hz), 5.28-5.38 (m, 2H), 4.39 (s, 2H), 4.00-4.15 (m, 1H), 3.81-3.91 (m, 1H), 3.46-3.60 (m, 2H), 3.33 (s, 3H), 2.21-2.33 (m, 1H), 1.74-1.90 (m, 1H), 1.41-1.58 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 148.0, 138.5, 134.8, 133.7, 133.1, 132.4, 131.1, 129.1, 128.5, 127.7, 127.6, 125.5, 75.2, 73.3, 70.8, 56.0, 53.0, 31.8, 29.9. Anal. Calcd. for $C_{21}H_{24}N_2O_6S$: C 58.32; H, 5.59; N, 6.47. Found: C, 58.24; H, 5.37; N, 6.08.

Methyl 6-O-benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-α-D,L-erithro-hex-2-enopyranoside (**22**)*:* a liquid, R_f= 0.28 [9:1 CH_2Cl_2/(*i*-Pr)$_2$O]; FTIR ν_{max}(liquid film) 3357, 1539, 1453, 1410, 1346, 1164, 1074, 935 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.09 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.82 (dd, 1H, *J* = 7.9, 1.5 Hz), 7.68 (dt, 1H, *J* = 7.6, 1.6 Hz), 7.60 (dt, 1H, *J* = 7.6, 1.5 Hz), 7.27-7.39 (m, 5H), 5.82-5.91 (m, 1H) 5.52 (dd, 1H, *J* = 9.9, 2.1 Hz), 5.42 (d, 1H, *J* = 8.7 Hz), 4.34 (s, 2H), 4.01-4.12 (m, 1H), 3.65 (dd, 1H, *J* = 7.7, 3.8 Hz), 3.53 (dd, 1H, *J* = 9.4, 4.3 Hz), 3.43 (dd, 1H, *J* = 9.4, 3.7 Hz), 3.33 (s, 3H), 1.93-2.03 (m, 1H), 1.54-1.80 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 147.9, 138.6, 134.9, 133.6, 133.0, 131.7, 130.9, 129.3, 127.7, 127.6, 127.5, 125.4, 73.1, 71.6, 70.5, 56.8, 52.7, 36.4, 29.5. Anal. Calcd. for $C_{21}H_{24}N_2O_6S$: C 58.32; H, 5.59; N, 6.47. Found: C, 58.46; H, 5.27; N, 6.11.

*3.4.2. Methanolysis of N-nosyl aziridine **9α-Ns** with 2.5·10^{-3} N TsOH/CH_2Cl_2 containing MeOH (6 equiv) (protocol B)*

N-nosyl aziridine **9α-Ns** (0.020 g, 0.050 mmol) was added to a CH_2Cl_2 solution (2.0 mL) containing MeOH (0.012 mL, 0.30 mmoli, 6.0 equiv) and TsOH·H_2O (0.001 g, 0.005 mmol, 0.1 equiv) (aziridine: TsOH: MeOH = 1: 0.1: 6) and the resulting mixture was stirred 18 h at room temperature. Dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product consisting of *trans*-3-methoxy-4-(*N*-nosylamino) derivative **20** (0.019 g, 90% yield) (entry 2, Table 1).

*3.4.3. Methanolysis of N-nosyl aziridine **9β-Ns** with 0.2 N H_2SO_4/MeOH (protocol A)*

N-nosyl aziridine **9β-Ns** (0.020 g, 0.050 mmol) was added to a 0.2 N H_2SO_4/MeOH (2.0 mL) and the resulting reaction mixture was stirred 2 h at room temperature. After dilution with CH_2Cl_2, solid $NaHCO_3$ was added. Evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution, afforded a crude product (0.020 g, 92% yield) consisting of *6-O-benzyl-3-O-methyl-4-deoxy-4-(N-nosylamino)-5a-carba-D,L-gulal* (**27**) (entry 1, Table 2), pure as a yellow liquid: R_f= 0.85 (9:1 CH_2Cl_2/(*i*-Pr)$_2$O, 2 runs); FTIR ν_{max}(liquid film) 3346, 1538, 1441, 1422, 1361, 1260, 1165, 1079, 1015 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.13-8.18 (m, 1H), 7.81-7.87 (m, 1H), 7.59-7.72 (m, 2H), 7.28-7.40 (m, 5H), 5.91 (dt, 1H, *J* = 10.0, 3.4 Hz), 5.64-5.76 (m, 2H), 4.35 (s, 2H), 3.89-3.98 (m, 1H), 3.45 (t, 1H, *J* = 3.7 Hz), 3.29-3.39 (m, 2H), 3.13 (s, 3H), 2.45 (dt, 1H, *J* = 5.8, 2.8 Hz), 2.14-2.32 (m, 1H), 1.81 (dd, 1H, *J* = 19.0, 8.8 Hz). ^{13}C NMR ($CDCl_3$) δ 147.9, 138.2, 135.2, 133.3, 132.9, 131.1, 130.9, 128.6, 127.8, 127.7, 125.3, 124.1, 76.5, 73.2, 70.6, 56.7, 52.9, 33.6, 25.6. Anal. Calcd. for $C_{21}H_{24}N_2O_6S$: C 58.32; H, 5.59; N, 6.47. Found: C, 58.19; H, 5.33; N, 6.54.

*3.4.4. Methanolysis of N-nosyl aziridine **9β-Ns** with $2.5 \cdot 10^{-3}$ N TsOH/CH_2Cl_2 containing MeOH (6 equiv) (protocol B)*

N-nosyl aziridine **9β-Ns** (0.060 g, 0.15 mmol) was added to a CH_2Cl_2 solution (6.0 mL) containing MeOH (0.036 mL, 0.90 mmoli, 6.0 equiv) and TsOH·H_2O (0.003 g, 0.015 mmoli, 0.1 equiv) (aziridine: TsOH: MeOH = 1: 0.1: 6) and the resulting mixture was stirred 18 h at room temperature. Dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (0.061 g, 94% yield) consisting of a 40:35:25 mixture of *N*-(nosylamino)-methoxy derivatives **27, 28** and **29** (^{1}H NMR) (entry 2, Table 2) which was subjected to preparative TLC using a 9:1 CH_2Cl_2/(*i*-Pr)$_2$O mixture as the eluant. Extraction of the three most intense bands afforded *trans*-3-methoxy-4-(*N*-nosylamino)- **27** (0.018 g, 28% yield), *trans*- **28** (0.014 g, 22% yield) and *cis*-1-methoxy-4-(*N*-nosylamino) derivative **29** (0.009 g, 14% yield).

Methyl 6-O-benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-α-D,L-threo-hex-2-enopyranoside (**28**): a liquid, R_f= 0.64 (9:1 CH_2Cl_2/(*i*-Pr)$_2$O, 2 runs); FTIR ν_{max}(liquid film) 3392, 1537, 1453, 1416, 1359, 1259, 1164, 1094, 1077, 1012 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.10-8.18 (m, 1H), 7.80-7.88 (m, 1H), 7.62-7.74 (m, 2H), 7.27-7.40 (m, 5H), 5.88 (dd, 1H, *J* = 10.1, 4.2 Hz), 5.76 (d, 1H, *J* = 7.8 Hz), 5.64 (dd, 1H, *J* = 10.1, 4.2 Hz), 4.45 (d, 1H, *J* = 12.0 Hz), 4.39 (d, 1H, *J* = 12.0 Hz), 4.07-4.22

(m, 1H), 3.69 (dd, 1H, *J* = 8.0, 4.0 Hz), 3.57 (dd, 1H, *J* = 9.4, 7.8 Hz), 3.41 (dd, 1H, *J* = 9.1, 5.4 Hz), 3.32 (s, 3H), 2.29-2.46 (m, 1H), 1.83 (dt, 1H, *J* = 14.1, 3.3 Hz), 1.61-1.71 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 147.9, 138.1, 133.5, 135.1, 133.1, 130.9, 129.9, 129.8, 128.6, 127.9, 125.5, 73.3, 71.8, 70.8, 56.6, 50.8, 34.5, 27.3. Anal. Calcd. for $C_{21}H_{24}N_2O_6S$: C 58.32; H, 5.59; N, 6.47. Found: C, 58.02; H, 5.24; N, 6.12.

Methyl 6-O-benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-β-D,L-threo-hex-2-enopyranoside (**29**): a liquid, R_f= 0.60 (9:1 CH_2Cl_2/(*i*-Pr)$_2$O, 2 runs); FTIR ν_{max}(liquid film) 3341, 1538, 1453, 1420, 1347, 1260, 1166, 1087 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.11-8.16 (m, 1H), 7.81-7.88 (m, 1H), 7.62-7.75 (m, 2H), 7.27-7.40 (m, 5H), 5.78-5.85 (m, 1H), 5.55 (d, 1H, *J* = 8.6 Hz), 5.43 (ddd, 1H, *J* = 10.0, 4.8, 2.0 Hz), 4.47 (d, 1H, *J* = 12.0 Hz), 4.40 (d, 1H, *J* = 12.0 Hz), 4.07-4.19 (m, 1H), 3.71-3.82 (m, 1H), 3.59-3.71 (m, 1H), 3.36-3.45 (m, 1H), 3.34 (s, 3H), 2.22-2.48 (m, 1H), 1.92-2.16 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 147.9, 138.3, 135.3, 133.6, 132.9, 130.9, 130.7, 129.8, 128.6, 127.9, 127.8, 125.5, 75.0, 73.5, 71.6, 56.2, 50.6, 36.9, 27.3. Anal. Calcd. for $C_{21}H_{24}N_2O_6S$: C 58.32; H, 5.59; N, 6.47. Found: C, 58.13; H, 5.74; N, 6.29.

*3.5. Reaction of aziridines **9α-Ns** and **9β-Ns** with AcOH (O-nucleophile) under basic and acid conditions*

*3.5.1. Acetolysis of aziridine **9α-Ns** with AcONa in 20% aqueous DMF (protocol B)*

AcONa (0.049 g, 0.60 mmol, 4.0 equiv) was added to a solution of *N*-nosyl aziridine **9α-Ns** (0.060 g, 0.15 mmol) in 20% aqueous DMF (3.5 mL) and the resulting reaction mixture was stirred 2 h at room temperature. Dilution with Et_2O and evaporation of the washed (brine) organic solution afforded a crude reaction product (0.067 g) mainly consisting of *trans* 3-acetoxy-4-(*N*-nosylamino)-derivative **23** (entry 6, Table 1), which was subjected to flash chromatography. Elution with a 1:1 hexane/AcOEt mixture afforded *3-O-acetyl-6-O-benzyl-4-deoxy-4-(N-nosylamino)-5a-carba-D,L-glucal* (**23**) (0.054 g, 78% yield), pure as a pale yellow liquid: R_f= 0.40 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3348, 1727, 1536, 1442, 1342, 1259, 1162, 1074, 1026 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.09-8.15 (m, 1H), 7.83-7.88 (m, 1H), 7.59-7.72 (m, 2H), 7.27-7.39 (m, 5H), 5.79-5.88 (m, 1H), 5.42-5.52 (m, 2H), 5.30 (d, 1H, *J* = 8.7 Hz), 4.38 (d, 1H, *J* = 11.7 Hz), 4.30 (d, 1H, *J* = 11.7 Hz), 3.85 (dd, 1H, *J* = 14.0, 8.7 Hz), 3.60 (dd, 1H, *J* = 9.4, 4.1 Hz), 3.49 (dd, 1H, *J* = 9.4, 5.3 Hz), 2.29-2.45 (m, 1H), 2.10-2.26 (m, 2H), 1.61 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 170.6, 147.7, 138.3, 135.9, 133.2, 133.1, 130.6, 130.0, 128.5, 127.7, 127.6, 125.3, 125.0, 73.4, 73.1, 70.9, 56.6, 39.0, 29.0, 20.7. Anal. Calcd. for $C_{22}H_{24}N_2O_7S$: C 57.38; H, 5.25; N, 6.08. Found: C, 57.06; H, 5.34; N, 5.87.

3.5.2. Acetolysis of N-nosyl aziridine ***9α-Ns*** *with 0.2 N H_2SO_4/AcOH (protocol A)*

N-nosyl aziridine **9α-Ns** (0.060 g, 0.15 mmol) was added to a 0.2 N H_2SO_4/AcOH (3.0 mL) and the reaction mixture was stirred 1 h at room temperature. Dilution with Et_2O and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (0.067 g, 97% yield) consisting of an 8:22:45:25 mixture of *trans*- **23** and *cis*-3-acetoxy-4-(*N*-nosylamino)- **24**, *trans*- **25** and *cis*-1-acetoxy-4-(*N*-nosylamino) derivative **26** (^{1}H NMR) (entry 4, Table 1), which was subjected to preparative TLC using a 9:1 CH_2Cl_2/(*i*-Pr)$_2$O mixture as the eluant. Extraction of the three most intense bands afforded *cis*-3acetoxy-4-(*N*-nosylamino)- **24** (0.012 g, 17% yield), *trans*- **25** (0.021 g, 30% yield) and *cis*-1-acetoxy-4-(*N*-nosylamino) derivative **26** (0.010 g, 14% yield).

3-O-acetyl-6-O-benzyl-4-deoxy-4-(N-nosylamino)-5a-carba-D,L-altral (**24**), a colourless oil: FTIR ν_{max}(liquid film) 3494, 1731, 1540, 1413, 1259, 1093, 1018 cm^{-1}; ^{1}H NMR δ 8.10-8.15 (m, 1H), 7.83-7.88 (m, 1H), 7.67-7.76 (m, 2H), 7.29-7.40 (m, 5H), 5.90-5.98 (m, 1H), 5.83, (d, 1H, *J* = 9.1 Hz), 5.57-5.66 (m, 1H), 4.72 (t, 1H, *J* = 4.3 Hz), 4.52 (s, 2H), 3.79-3.90 (m, 1H), 3.58-3.71 (m, 2H), 2.32-2.46 (m, 1H), 2.15-2.28 (m, 2H), 1.93 (s, 3H). ^{13}C NMR δ 170.2, 147.9, 138.5, 133.9, 133.4, 130.6, 128.6, 128.0, 127.8, 125.7, 123.5, 73.6, 70.8, 67.5, 54.3, 34.8, 31.8, 22.9. Anal. Calcd. for $C_{22}H_{24}N_2O_7S$: C 57.38; H, 5.25; N, 6.08. Found: C, 57.21; H, 5.09; N, 6.00.

6-O-Benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-β-D,L-erithro-hex-2-enopyranosyl acetate (**25**), a colourless oil: FTIR ν_{max}(liquid film) 3335, 1726, 1539, 1441, 1417, 1360, 1259, 1165, 1068, 1020 cm^{-1}. ^{1}H NMR δ 8.10 (dd, 1H, *J* = 7.6, 1.5 Hz), 7.25 (dd, 1H, *J* = 7.6, 1.5 Hz), 7.56-7.78 (m, 2H), 7.28-7.41 (m, 5H), 5.61-5.70 (m, 1H), 5.44 (dt, 1H, *J* = 10.2, 2.1 Hz), 5.35 (d, 1H, *J* = 8.7 Hz), 5.29-5.40 (m, $W_{1/2}$= 15.4 Hz, 1H), 4.36 (s, 2H), 4.11-4.27 (m, 1H), 3.56 (dd, 1H, *J* = 9.1, 4.3 Hz), 3.42 (dd, 1H, *J* = 9.1, 3.3 Hz), 2.13-2.34 (m, 1H), 2.02 (s, 3H), 1.81-1.97 (m, 1H), 1.60-1.78 (m, 1H). ^{13}C NMR δ 170.7, 148.0, 138.4, 134.8, 133.7, 133.1, 131.0, 130.8, 130.7, 128.5, 127.8, 127.6, 125.5, 73.3, 70.2, 69.2, 52.4, 40.9, 31.6, 22.8. Anal. Calcd. for $C_{22}H_{24}N_2O_7S$: C 57.38; H, 5.25; N, 6.08. Found: C, 57.10; H, 4.94; N, 5.69.

6-O-Benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-α-D,L-erithro-hex-2-enopyranosyl acetate (**26**), a colourless oil: FTIR ν_{max}(liquid film) 3494, 1731, 1540, 1413, 1259, 1093, 1018 cm^{-1}. ^{1}H NMR δ 8.10 (dd, 1H, *J* = 7.6, 1.5 Hz), 7.85 (dd, 1H, *J* = 7.7, 1.5 Hz), 7.58-7.75 (m, 2H), 7.27-7.40 (m, 5H), 5.81 (ddd, 1H, *J* = 9.6, 4.3, 2.0 Hz), 5.59 (dd, 1H, *J* = 9.6, 2.2 Hz), 5.41 (d, 1H, *J* = 8.5 Hz), 5.14-5.20 (m, 1H), 4.34 (s, 2H), 4.05-4.15 (m, 1H), 3.55 (dd, 1H, *J* = 9.4, 4.1 Hz), 3.45 (dd,

1H, *J* = 9.4, 3.5 Hz), 2.04 (s, 3H), 1.95-2.02 (m, 1H), 1.86-1.95 (m, 2H). ^{13}C NMR δ 170.7, 148.0, 138.4, 134.8, 133.7, 133.3, 133.2, 131.0, 128.6, 127.8, 127.7, 125.5, 73.3, 70.3, 65.6, 52.4, 36.8, 30.5, 21.4. Anal. Calcd. for $C_{22}H_{24}N_2O_7S$: C 57.38; H, 5.25; N, 6.08. Found: C, 57.22; H, 5.04; N, 5.95.

3.5.3. Acetolysis of N-nosyl aziridine ***9α-Ns*** *with* $2.5 \cdot 10^{-3}$ *N TsOH/CH_2Cl_2 containing AcOH (6 equiv) (protocol B)*

N-nosyl aziridine **9α-Ns** (0.020 g, 0.050 mmol) was treated with $2.5 \cdot 10^{-3}$ N TsOH/CH_2Cl_2 solution (0.5 mL) containing AcOH (0.018 g, 0.017 mL, 0.30 mmol, 6 equiv) and the reaction mixture was stirred 16 h at room temperature. Usual work-up afforded a crude reaction product consisting of 11:29:19:41 mixture of *trans*- **23** and *cis*-3-acetoxy-4-(*N*-nosylamino)- **24**, *trans*- **25** and *cis*-1-acetoxy-4-(*N*-nosylamino) derivative **26** (^{1}H NMR) (entry 5, Table 1).

3.5.4. Acetolysis of N-nosyl aziridine ***9β-Ns*** *with AcONa in 20% aqueous DMF (protocol B)*

AcONa (0.050 g, 0.60 mmol, 4.0 equiv) was added to a solution of *N*-nosyl aziridine **9β-Ns** (0.060 g, 0.15 mmol) in 20% aqueous DMF (3.5 mL) and the resulting reaction mixture was stirred 2 h at room temperature. Dilution with Et_2O and evaporation of the washed (brine) organic solution afforded a crude reaction product (0.068 g) mainly consisting of *trans*-3-acetoxy-4-(*N*-nosylamino) derivative **30** (entry 6, Table 2) which was subjected to flash chromatography. Elution with a 1:1 hexane/AcOEt mixture afforded *3-O-acetyl-6-O-benzyl-4-deoxy-4-(N-nosylamino)-5*a*-carba-D,L-gulal* (**30**) (0.052 g, 75% yield), pure as a pale yellow liquid: R_f= 0.45 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3361, 1731, 1539, 1441, 1424, 1362, 1258, 1236, 1166, 1090, 1013 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.15-8.24 (m, 1H), 7.80-7.90 (m, 1H), 7.67, 7.77 (m, 2H), 7.29-7.43 (m, 5H), 5.97-6.07 (m, 1H), 5.56-5.74 (m, 2H), 4.90 (t, 1H, *J* = 3.9 Hz), 4.51 (d, 1H, *J* = 12.0 Hz), 4.42 (d, 1H, *J* = 12.0 Hz), 3.95 (dt, 1H, *J* = 9.1, 3.4 Hz), 3.48-3.59 (m, 1H), 3.42 (dd, 1H, *J* = 9.1, 5.7 Hz), 2.10-2.51 (m, 2H), 1.93 (s, 3H), 1.77-1.92 (m, 1H). ^{13}C NMR δ 170.2, 147.0, 138.3, 134.2, 133.7, 133.0, 132.4, 131.4, 128.6, 128.0, 125.4, 122.7, 73.5, 70.6, 68.1, 53.0, 33.7, 29.9, 21.2. Anal. Calcd. for $C_{22}H_{24}N_2O_7S$: C 57.38; H, 5.25; N, 6.08. Found: C, 57.54; H, 5.18; N, 6.03.

3.5.5. Acetolysis of N-nosyl aziridine ***9β-Ns*** *with 0.2 N H_2SO_4/AcOH (protocol A)*

N-nosyl aziridine **9β-Ns** (0.040 g, 0.10 mmol) was added to a 0.2 N H_2SO_4/AcOH solution (2.0 mL) and the reaction mixture was stirred 1 h at room temperature. Dilution with Et_2O and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (0.045 g, 98% yield) consisting of a 36:64 mixture of *trans*-3-acetoxy-4-(*N*-

nosylamino)- **30** and *trans*-1-acetoxy-4-(*N*-nosylamino) derivative **31** (^{1}H NMR) (entry 4, Table 2) which was subjected to preparative TLC using a 9:1 CH_2Cl_2/(*i*-Pr)$_2$O mixture as the eluant. Extraction of the two most intense bands afforded *trans*-3-acetoxy-4-(*N*-nosylamino) derivative **30** (0.010 g, 22% yield) and *6-O-benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-α-D,L-threo-hex-2-enopyranosyl acetate* (**31**) (0.019 g, 41% yield) pure as a pale yellow oil: R_f = 0.53 (9:1 CH_2Cl_2/(*i*-Pr)$_2$O); FTIR ν_{max}(liquid film) 3261, 1731, 1539, 1441, 1424, 1362, 1258, 1236, 1166, 1090, 1013 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.08-8.16 (m, 1H), 7.78-7.87 (m, 1H), 7.62-7.74 (m, 2H), 7.27-7.40 (m, 5H), 5.77-5.85 (m, 1H), 5.65-5.77 (m, 2H), 5.21 (dd, 1H, *J* = 7.9, 3.9 Hz), 4.51 (d, 1H, *J* = 12.0 Hz), 4.42 (d, 1H, *J* = 12.0 Hz), 4.10-4.26 (m, 1H), 3.60 (dd, 1H, *J* = 9.3, 8.1 Hz), 3.43 (dd, 1H, *J* = 9.3, 5.3 Hz), 2.29-2.47 (m, 1H), 2.00 (s, 3H), 1.71-1.85 (m, 2H). ^{13}C NMR δ 170.6, 148.0, 138.3, 133.6, 133.2, 133.1, 131.4, 130.8, 128.7, 128.3, 128.0, 127.9, 125.6, 73.7, 70.9, 65.9, 50.6, 35.0, 28.1, 21.6. Anal. Calcd. for $C_{22}H_{24}N_2O_7S$: C 57.38; H, 5.25; N, 6.08. Found: C, 57.14; H, 4.93; N, 5.81.

*3.5.6. Acetolysis of N-nosyl aziridine **9β-Ns** with 2.5·10^{-3} N TsOH/CH_2Cl_2 containing AcOH (6 equiv) (protocol B)*

N-nosyl aziridine **9β-Ns** (0.020 g, 0.050 mmol) was treated with 2.5·10^{-3} N TsOH/CH_2Cl_2 solution (0.5 mL) containing AcOH (0.018 g, 0.017 mL, 0.30 mmol, 6 equiv) and the reaction mixture was stirred 18 h at room temperature. Dilution with Et_2O and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (0.021 g, 91% yield) consisting of a 30:70 mixture of *trans*-3-acetoxy-4-(*N*-nosylamino)- **30** and *trans*-1-acetoxy-4-(*N*-nosylamino) derivative **31** (^{1}H NMR) (entry 5, Table 2).

*3.6. Acid methanolysis of epoxides **1α** and **1β** and N-nosyl aziridines **9α-Ns** and **9β-Ns** in the presence of an ionic liquid (IL)*

*3.6.1. Acid methanolysis of epoxide **1α** with 2.5·10^{-3} N TsOH in 1:1 CH_2Cl_2/[bmim][BF_4] solution containing MeOH (6 equiv) (protocol B)*

Typical procedure. A solution of epoxide **1α** (0.011 g, 0.051 mmol) in 2.5·10^{-3} N TsOH in 1:1 CH_2Cl_2/[bimim][BF_4] mixture (1.0 mL) containing MeOH (12.0 μL, 0.0098 g, 0.306 mmol, 6 equiv) was stirred 18 h at room temperature. Dilution with Et_2O and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (0.012 g, 97% yield) consisting of a 20:76:4 mixture of corresponding methoxy alcohols derivatives **3** (*anti*-

1,2-addition product), **4** (*syn-1,4-addition product)* and **5** (*anti-1,4-addition product*),[9a] respectively (^{1}H NMR) (entry 4, Table 3).

*3.6.2. Methanolysis of epoxide **1β** with $2.5 \cdot 10^{-3}$ N TsOH in 1:1 CH_2Cl_2/[bmim][BF_4] solution containing MeOH (6 equiv) (protocol B)*

Following the typical procedure, a solution of epoxide **1β** (0.011 g, 0.051 mmol) in $2.5 \cdot 10^{-3}$ N TsOH in 1:1 CH_2Cl_2/[bimim][BF_4] mixture (1.0 mL) containing MeOH (12.0 μL, 0.0096 g, 0.306 mmol, 6 equiv) was stirred 18 h at room temperature. Usual workup afforded a crude reaction product (0.011 g, 89% yield) consisting of a 51:31:18 mixture of corresponding methoxy alcohols derivatives **6** (*anti-1,2-addition product*), **7** (*syn-1,4-addition product)* and **8** (*anti-1,4-addition product*),,[9a] respectively (^{1}H NMR) (entry 4, Table 4).

*3.6.3. Methanolysis of N-nosyl aziridine **9α-Ns** with $2.5 \cdot 10^{-3}$ N TsOH in 1:1 CH_2Cl_2/[bmim][BF_4] solution containing MeOH (6 equiv) (protocol B)*

Typical procedure. A solution of *N*-nosyl aziridine **9α-Ns** (0.010 g, 0.025 mmol) in $2.5 \cdot 10^{-3}$ N TsOH in CH_2Cl_2/[bimim][BF_4] mixture (1:1) (1.0 mL) containing MeOH (6.0 μL, 0.15 mmol, 6 equiv) was stirred 18 h at room temperature. Dilution with Et_2O and evaporation of the washed (saturated aqueous $NaHCO_3$ and brine) organic solution afforded a crude reaction product (0.010 g, 99% yield**)** consisting of *trans*-3-methoxy-4-(*N*-nosylamino) derivative **20** (^{1}H NMR) (entry 3, Table 1).

*3.6.4. Methanolysis of N-nosyl aziridine **9β-Ns** with $2.5 \cdot 10^{-3}$ N TsOH in 1:1 CH_2Cl_2/[bmim][BF_4] solution containing MeOH (6 equiv) (protocol B)*

Following the typical procedure, a solution of *N*-nosyl aziridine **9β-Ns** (0.010 g, 0.025 mmol) in $2.5 \cdot 10^{-3}$ N TsOH in 1:1 CH_2Cl_2/[bimim][BF_4] mixture (1.0 mL) containing MeOH (6.0 μL, 0.15 mmol, 6 equiv) was stirred 18 h at room temperature. Usual workup afforded a crude reaction product (0.010 g, 99% yield) consisting of a 40:28:32 mixture of *trans*-3-methoxy-4-(*N*-nosylamino)- **27**, *trans*- **28** and *cis*-1-methoxy-4-(*N*-nosylamino) derivative **29** (^{1}H NMR) (entry 3, Table 2).

*3.7. Reactions of N-nosyl aziridines **9α-Ns** and **9β-Ns** with NaN_3 and $NHEt_2$ (N-Nucleophiles)*

*3.7.1. Reaction of N-nosyl aziridine **9α-Ns** with NaN_3 in 1:1 THF/H_2O (protocol B)*

A solution of *N*-nosyl ziridine **9α-Ns** (0.033 g, 0.0825 mmol) in distilled THF (0.3 mL) was added to a solution of NaN_3 (0.0059 g, 0.091 mmol, 1.1 equiv) in H_2O (0.3 mL) and the reaction mixture was stirred 4 h at room temperature. After dilution with Et_2O, evaporation of the washed (brine) organic solution afforded a crude reaction product (0.035 g, 96% yield) consisting of 77:23 mixture of *trans*-3-azido-4-(*N*-nosylamino)- **34** and *trans*-1-azido-4-(*N*-nosylamino) derivative **35** which was subjected to preparative TLC, using a 7:3 hexane/AcOEt mixture as the eluant. Extraction of the two most intense bands afforded *trans*-3-azido-4-(*N*-nosylamino)- **34** (0.015 g, 41% yield) and *trans*-1-azido-4-(*N*-nosylamino) derivative **35** (0.005 g, 14% yield).

6-O-Benzyl-3,4-dideoxy-3-azido-4-(N-nosylamino)-5a-carba-D,L-glucal (**34**)*:* a colourless liquid, R_f= 0.56 (7:3 hexane/AcOEt); FTIR ν_{max}(liquid film) 3334, 2094, 1536, 1422, 1358, 1257, 1165, 1119, 1084, 1061, 1027, 916 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.16-8.21 (m, 1H), 7.83-7.93 (m, 1H), 7.66-7.76 (m, 2H), 7.27-7.41 (m, 5H), 5.85-5.95 (m, 1H), 5.60 (d, 1H, *J* = 9.0 Hz), 5.51 (d, 1H, *J* = 9.0 Hz), 4.50 (d, 1H, *J* = 11.7 Hz), 4.44 (d, 1H, *J* = 11.7 Hz), 3.72-3.79 (m, 1H), 3.68 (dd, 1H, *J* = 9.7, 4.2 Hz), 3.50-3.62 (m, 2H), 2.30-2.44 (m, 1H), 2.16-2.26 (m, 1H), 2.00-2.15 (m, 1H). ^{13}C NMR (CD_3CN) δ 140.4, 136.1, 134.8, 133.3, 132.4, 132.0, 130.6, 129.9, 129.1, 126.9, 125.6, 74.2, 71.5, 58.5, 53.4, 41.4, 33.0. Anal. Calcd. for $C_{20}H_{21}N_5O_5S$: C 54.16; H, 4.77; N, 15.79. Found: C, 54.09; H, 4.54; N, 15.55.

6-O-Benzyl-4-(N-nosylamino)-2,3,4-trideoxy-5a-carba-β-D,L-erithro-hex-2-enopyranosyl azide (**35**)*:* a colourles liquid, R_f= 0.36 (7:3 hexane/AcOEt); FTIR ν_{max}(liquid film) 3354, 2094, 1646, 1540, 1453, 1356, 1257, 1167, 1093, 1062 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.11 (dd, 1H, *J* = 7.3, 2.1 Hz), 7.83-7.88 (m, 1H), 7.62-7.76 (m, 2H), 7.27-7.41 (m, 5H), 5.69 (ddd, 1H, *J* = 10.1, 2.3, 1.8 Hz), 5.45 (dt, 1H, *J* = 10.1, 2.2 Hz), 5.36 (d, 1H, *J* = 8.7 Hz), 4.39 (s, 2H), 4.04-4.22 (m, 1H), 3.87-4.03 (m, 1H), 3.54 (d, 2H, *J* = 4.2 Hz), 2.20-2.30 (m, 1H), 1.61-1.89 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 147.9, 138.3, 134.7, 133.8, 133.2, 131.2, 131.0, 130.0, 128.6, 127.9, 127.7, 125.5, 73.4, 70.2, 57.0, 52.4, 41.1, 31.8. Anal. Calcd. for $C_{20}H_{21}N_5O_5S$: C 54.16; H, 4.77; N, 15.79. Found: C, 54.29; H, 4.49; N, 15.39.

*3.7.2. Reaction of N-nosyl aziridine **9β-Ns** with NaN_3 in 1:1 THF/H_2O (protocol B)*

A solution of *N*-nosyl aziridine **9β-Ns** (0.022 g, 0.055 mmol) in distilled THF (0.2 mL) was added to a solution of NaN_3 (0.004 g, 0.061 mmol, 1.1 equiv) in H_2O (0.2 mL) and the reaction mixture was stirred 4 h at room temperature. After dilution with Et_2O, evaporation of the washed (brine) organic solution afforded a reaction product (0.023 g, 99% yield) consisting of *trans*-3-

azido-4-(*N*-nosylamino) derivative **37** (0.020 g) which was subjected to preparative TLC using a 7:3 hexane/AcOEt mixture as the eluant. Extraction of the most intense band afforded pure *6-O-benzyl-3,4-dideoxy-3-azido-4-(N-nosylamino)-5a-carba-D,L-gulal* (**37**), (0.021 g, 86% yield), a liquid, R_f= 0.39 (hexane/AcOEt 7:3); FTIR ν_{max}(liquid film) 3342, 2096, 1538, 1442, 1422, 1360, 1242, 1166, 1098, 1078, 1012 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.10-8.19 (m, 1H), 7.79-7.89 (m, 1H), 7.61-7.74 (m, 2H), 7.27-7.41 (m, 5H), 6.00-6.10 (m, 1H), 6.90 (d, 1H, *J* = 8.5 Hz), 5.60-5.70 (m, 1H), 4.34 (s, 2H), 3.80-3.90 (m, 1H), 3.72 (t, 1H, *J* = 3.7 Hz), 3.31-3.46 (m, 2H), 2.19-2.47 (m, 2H), 1.76-1.94 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 147.9, 137.9, 134.8, 133.6, 133.1, 132.4, 130.9, 128.6, 127.9, 127.6, 125.5, 122.0, 73.3, 70.3, 59.1, 54.5, 33.9, 25.5. Anal. Calcd. for $C_{20}H_{21}N_5O_5S$: C 54.16; H, 4.77; N, 15.79. Found: C, 54.11; H, 4.91; N, 15.74.

*3.7.3. Reaction of N-nosyl aziridine **9α-Ns** with Et_2NH (protocol A)*

N-nosyl aziridine **9α-Ns** (0.015 g, 0.0375 mmol) was dissolved in distilled Et_2NH (1.5 mL) and the reaction mixture was stirred at room temperature for 2 days in the presence of $Sc(OTf)_3$ (0.0018 g, 0.00375 mmol, 0.1 equiv). Dilution with Et_2O and evaporation of the washed (brine) organic solution afforded a reaction product (0.016 g, 90% yield) consisting of *trans*-3-(*N,N*-diethylamino)-4-(*N*-nosylamino) derivative **33** which was subjected to preparative TLC, using a 6:4 hexane/AcOEt mixture as the eluant. Extraction of the most intense band afforded *6-O-benzyl-3,4-dideoxy-3-(N,N-diethylamino)-4-(N-nosylamino)-5a-carba-D,L-glucal* (**33**) (0.012 g, 68% yield), pure as a pale yellow liquid: R_f= 0.38 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3372, 1542, 1460, 1401, 1347, 1304, 1170, 1120, 1065, 1055 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.09-8.20 (m, 1H), 7.84-7.93 (m, 1H), 7.60-7.70 (m, 2H), 7.28-7.39 (m, 5H), 5.71-5.84 (m, 1H), 5.50-5.60 (m, 1H), 4.51 (d, 1H, *J* = 11.9 Hz), 4.44 (d, 1H, *J* = 11.9 Hz), 3.75 (dd, 1H, *J* = 9.0, 3.4 Hz), 3.47-3.64 (m, 2H), 3.07-3.20 (m, 1H, $W_{1/2}$ = 17.8 Hz), 2.15-2.41 (m, 6H), 1.95-2.09 (m, 2H), 0.67 (t, 6H, *J* = 7.1 Hz). ^{13}C NMR ($CDCl_3$) δ 147.7, 138.7, 137.0, 132.9, 132.7, 130.8, 128.7, 128.5, 127.9, 127.7, 126.0, 125.4, 73.4, 72.6, 64.2, 57.0, 43.9, 41.2, 29.7, 13.3. Anal. Calcd. for $C_{24}H_{31}N_3O_5S$: C 60.86; H, 6.60; N, 8.87. Found: C, 60.48; H, 6.28; N, 8.50.

*3.7.4. Reaction of N-nosyl aziridine **9β-Ns** with Et_2NH (protocol A)*

N-nosyl aziridine **9β-Ns** (0.015 g, 0.0375 mmol) was dissolved in distilled Et_2NH (1.5 mL) and the reaction mixture was stirred at room temperature for 4 days in the presence of $Sc(OTf)_3$ (0.0018 g, 0.00375 mmol, 0.1 equiv). Dilution with Et_2O and evaporation of the washed (brine) organic solution afforded a reaction product (0.017 g, 96% yield) consisting of *trans*-3-(*N,N*-diethylamino)-4-(*N*-nosylamino) derivative **36** (^1H NMR) which was subjected to preparative TLC,

using a 6:4 hexane/AcOEt mixture as the eluant. Extraction of the most intense band afforded *6-O-benzyl-3,4-dideoxy-3-(N,N-diethylamino)-4-(N-nosylamino)-5a-carba-D,L-gulal* (**36**) (0.011 g, 62% yield), pure as a pale yellow liquid, R_f= 0.21 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3372, 1541, 1454, 1406, 1347, 1304, 1170, 1120, 1065, 1055 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.05-8.12 (m, 1H), 7.78-7.85 (m,1H), 7.57-7.85 (m, 2H), 7.27-7.35 (m, 5H), 5.71-5.82 (m, 1H), 5.48-5.58 (m, 1H), 4.43 (d, 1H, *J* = 12.1 Hz), 4.36 (d, 1H, *J* = 12.1 Hz), 3.48-3.70 (m, 2H), 3.45 (t, 1H, *J* = 9.6 Hz), 2.92-3.06 (m, 1H, $W_{1/2}$ = 10.8 Hz), 2.70-2.85 (m,1H), 2.33 (q, 4H, *J* = 6.6 Hz), 1.91-2.27 (m, 3H), 0.72 (t, 6H, *J* = 6.6 Hz). ^{13}C NMR ($CDCl_3$) δ 138.7, 134.7, 133.4, 132.8, 131.0, 129.2, 128.5, 127.9, 127.7, 127.6, 125.5, 125.1, 77.4, 73.1, 69.7, 59.1, 43.8, 35.0, 26.4, 13.3. Anal. Calcd. for $C_{24}H_{31}N_3O_5S$: C 60.86; H, 6.60; N, 8.87. Found: C, 60.59; H, 6.39; N, 8.66.

*3.8. Catalytic dihydroxylation of diastereoisomeric trans-3-methoxy-4-(N-nosylamino) derivatives **20** and **27** (anti-1,2-addition products) obtained by aziridines **9α-Ns** and **9β-Ns**, respectively*

*3.8.1.Catalytic dihydroxylation by OsO_4/NMO protocol of trans-3.methoxy-4-(N-nosylamino) derivative **20***

Typical procedure. A solution of *trans*-3-methoxy-4-(*N*-nosylamino) derivative **20** (0.030 g, 0.070 mmol) in an 1:1 *t*-BuOH/acetone mixture (0.24 mL) was added, at 0°C under stirring and in the dark, to a 50% p/v aqueous solution of *N*-methyl morpholine-*N*-oxide (NMO) (0.060 mL) and the resulting reaction mixture was treated with 2.5% p/v OsO_4 solution in *t*-BuOH (0.060 mL) and stirred for 15 h at room temperature. Dilution with Et_2O and evaporation of the filtered (Celite®) organic solution afforded a crude reaction product (0.032 g) consisting of *cis* diol **42** which was subjected to preparative TLC using a 9:1 CH_2Cl_2/(*i*-Pr)$_2$O mixture as the eluant. Extraction of the most intense band afforded pure *6-O-benzyl-3-O-methyl-4-deoxy-4-(N-nosylamino)-5a-carba-α-D,L-glucopyranose* (**42**), as a pale yellow oil (0.024 g, 73% yield): FTIR ν_{max}(liquid film) 3360 (broad), 1595, 1537, 1417, 1259, 1162, 1088, 1027, 798 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.09-8.16 (m, 1H), 7.77-7.88 (m, 1H), 7.56-7.74 (m, 2H), 7.28-7.41 (m, 5H), 5.40 (d, 1H, *J* = 9.4 Hz), 4.41 (d, 1H, *J* = 11.7 Hz), 4.36 (d, 1H, *J* = 11.7 Hz), 3.98-4.09 (m, 1H), 3.72 (t, 1H, *J* = 4.6 Hz), 3.52-3.57 (m, 2H), 3.47 (dd, 1H, *J* = 8.4, 2.4 Hz), 3.21 (t, 1H, *J* = 9.4 Hz), 2.97 (s, 3H), 2.37-2.44 (m, 1H), 1.94-2.12 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 147.0, 138.6, 136.3, 133.0, 132.8, 131.0, 128.7, 128.5, 127.8, 125.0, 84.0, 76.1, 73.3, 70.4, 69.0, 60.5, 58.3, 55.6, 37.1, 30.5, 29.9. Anal. Calcd. for $C_{21}H_{26}N_2O_8S$: C 54.06; H, 5.61; N, 6.60. Found: C, 53.75; H, 5.37; N, 6.55.

A solution of *cis* diol **42** (0.019 g, 0.040 mmol) in anhydrous pyridine (1.0 mL) was treated with Ac_2O (0.5 mL) at 0°C and the resulting reaction mixture was stirred at room temperature overnight. Co-evaporation of the reaction mixture with toluene afforded a crude product (0.021 g) consisting of diacetate **42-diAc**, which was subjected to preparative TLC, using a 1:1 hexane/AcOEt mixture as the eluant. Extraction of the more intense band afforded *1,2-di-O-acetyl-6-O-benzyl-3-O-methyl-4-deoxy-4-(N-nosylamino)-5a-carba-α-D,L-glucopyranose* (**42-diAc**) (0.016 g, 73% yield) pure as a pale yellow liquid: R_f = 0.30 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3228, 1736, 1718 (shoulder), 1537, 1454, 1366, 1344, 1249, 1238, 1163, 1075, 1047, 1024, 921 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.07-8.15 (m, 1H), 7.81-7.88 (m, 1H), 7.63-7.75 (m, 2H), 7.27-7.40 (m, 5H), 5.38 (d, 1H, *J* = 8.7 Hz), 5.32-5.37 (m, 1H), 4.71 (dd, 1H, *J* = 9.7, 2.9 Hz), 4.54 (d, 1H, *J* = 11.7 Hz), 4.45 (d, 1H, *J* = 11.7 Hz), 3.59-3.69 (m, 2H), 3.53 (t, 1H, *J* = 9.7 Hz), 3.28 (t, 1H, *J* = 9.7 Hz), 2.72 (s, 3H), 2.09 (s, 3H), 1.97 (s, 3H),1.66-1.77 (m, 1H), 1.55-1.65 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 170.1, 170.0, 147.8, 138.4, 136.2, 133.1, 132.8, 131.4, 128.5, 128.0, 127.8, 124.9, 81.4, 75.7, 73.5, 70.1, 68.9, 60.1, 58.5, 37.8, 29.9, 21.3, 21.1. Anal. Calcd. for $C_{25}H_{30}N_2O_{10}S$: C 54.54; H, 5.49; N, 5.08. Found: C, 54.30; H, 5.23; N, 4,73.

*3.8.2. Catalytic dihydroxylation by OsO_4/NMO protocol of trans-3-acetoxy-4-(N-nosylamino) derivative **27***

Following the typical procedure, the treatment of a solution of *trans*-3-acetoxy-4-(*N*-nosylamino) derivative **27** (0.030 g, 0.070 mmol) in an 1:1 *t*-BuOH/acetone mixture (0.24 mL) with 50% p/v aqueous solution of *N*-methyl morpholine-*N*-oxide (NMO) (0.060 mL) and 2.5% p/v OsO_4 solution in *t*-BuOH (0.060 ml) for 96 h at room temperature afforded a crude reaction product consisting of *cis* diol **43** (0.031 g): FTIR ν_{max}(liquid film) 3360 (broad), 1594 (broad), 1537, 1417,1259, 1162, 1088, 1027, 798 cm^{-1}. ^1H NMR (CD_3OD) δ 7.98-8.04 (m, 1H), 7.57-7.67 (m, 2H), 7.24-7.37 (m, 6H), 4.50-4.53 (m, 1H), 4.34 (d, 1H, *J* = 11.9 Hz), 4.27 (d, 1H, *J* = 11.9 Hz), 3.72-3.80 (m, 2H), 3.61-3.71 (m, 2H), 3.34-3.47 (m, 2H), 3.25 (s, 3H), 1.95-2.12 (m, 1H), 1.56-1.79 (m, 2H).

Di-*O*-acetylation of crude *cis* diol **43** (0.031 g, 0.066 mmmol) by anhydrous pyridine (1.0 mL)/Ac_2O (0.5 mL) protocol afforded a crude product (0.035 g) consisting of diacetate **43-diAc** which was subjected to preparative TLC using an 1:1 hexane/AcOEt mixture as the eluant. Extraction of the most intense band afforded *1,2-di-O-acetyl-6-O-benzyl-3-O-methyl-4-deoxy-4-(N-nosylamino)-5a-carba-β-D,L-idopyranose* (**43-diAc**) (0.026 g, 72% yield), pure as a pale yellow liquid: R_f= 0.34 (1:1 hexane/AcOEt); FTIR ν_{max}(liquid film) 3345, 1739, 1539, 1428, 1370, 1259,

1166, 1086, 1018, 797 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.08 (dd, 1H, *J* = 7.7, 1.8 Hz), 7.85 (dd, 1H, *J* = 7.6, 1.5 Hz), 7.70 (dt, 1H, *J* = 7.6, 1.5 Hz), 7.62 (dt, 1H, *J* = 7.6, 1.8 Hz), 7.27-7.40 (m, 5H), 6.06 (d, 1H, *J* = 9.5 Hz), 5.39 (t, 1H, *J* = 3.1 Hz), 5.07 (ddd, 1H, *J* = 11.8, 4.7, 3.1 Hz), 4.33 (d, 1H, *J* = 12.0 Hz), 4.27 (d, 1H, *J* = 12.0 Hz), 3.92 (dt,1H, *J* = 9.6, 3.1 Hz), 3.46 (dd, 1H, *J* = 9.6, 7.6 Hz), 3.26-3.34 (m, 2H), 3.25 (s, 3H), 2.29-2.46 (m, 1H), 2.24 (s, 3H), 1.98 (s, 3H), 1.69-1.85 (m, 1H), 1.57-1.65 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 170.2, 169.9, 147.8, 138.4, 134.7, 133.6, 133.0, 130.9, 128.6, 127.8, 127.6, 125.5, 79.1, 73.1, 70.9, 69.3, 68.6, 58.3, 51.9, 35.1, 29.9, 24.3, 21.1. Anal. Calcd. for $C_{25}H_{30}N_2O_{10}S$: C 54.54; H, 5.49; N, 5.08. Found: C, 54.27; H, 5.12; N, 4.92.

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Appendix A: Supplementary data

Supplementary data related to this article can be found at…...

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9. a) Di Bussolo V, Frau I, Checchia L, Favero L, Pineschi M, Uccello-Barretta G, Balzano F, Roselli G, Renzi G, Crotti P. *Tetrahedron* 2011; 67:4696-4709 and references therein (racemic **1α** and **1β**).

b) Frau I, Di Bussolo V, Favero L, Pineschi M, Crotti P. *Chirality* 2011; 23:820-826 (enantiopure (3*S*,4*R*,5*R*)-**1α** and (3*R*,4*S*,5*R*)-**1β**).

10. *Protocol A* reaction conditions: epoxide **1α** (or **1β**) or aziridine **9α-Ns** (or **9β-Ns**) is dissolved in the solvent/nucleophile (MeOH, AcOH, Et_2NH, as an example) in the presence of a catalyst, if necessary (H_2SO_4, TsOH or a Lewis acid). Under these conditions, the nucleophilic addition reaction occurs in the presence of a large excess of nucleophile, solvent of the reaction. *Protocol B* reaction conditions: epoxide **1α** (or **1β**) or aziridine **9α-Ns** (or **9β-Ns**) is dissolved in a non-nucleophilic solvent (CH_2Cl_2, MeCN, as an example) containing the nucleophile (MeOH, AcOH, azide anion, 3-6 equiv). Under these conditions, the nucleophilic addition reaction occurs in the presence of only a small excess of nucleophile.

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12. Azidolysis of epoxides **1β** and **1α** by the commonly used NaN_3/NH_4Cl in $MeOH/H_2O$ protocol turned out to be not regioselective and the desired *anti-1,2-addition product* **12**, from **1β** (Scheme 3) and **16** from **1α** (Scheme 4) were obtained in a mixture with the corresponding *anti-1,4-addition product* (80:20 and 55:45 *anti-1,2-/anti-1,4-addition product* ratio from **1β** and **1α**, respectively) (see ref. 9a).

13. In the presence of MeOH, **9β'-Ns-H**:**9β"-Ns-H** protonated aziridine conformers ratio is identical (about 99:1) to that present under neutral conditions between corresponding

aziridine conformers **9β'-Ns** and **9β"-Ns (**Schemes 5 and 6 and Supplementary data, sections 4.1 and 4.4).

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15. The stereoelectronic requirements of the conjugate addition (S_N2'-type reaction) are satisfied by attack of the nucleophile at C(1)-carbon of C(1)-C(2) π system of vinyl aziridines **9α-Ns** and **9β-Ns**, in either of the two possible orientation (*syn* or *anti*) with respect to allyl C(3)-N aziridine bond, acting as the leaving group. This reaction property justifies the reason why an absence of stereoselectivity is often observed in the formation of *1,4-addition products*. See: Atkinson R. S. In *Stereoselective Synthesis*; Wiley: Chichester, England, 1995, pp 110-111.

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17. Regioisomeric nucleophilic attack at C(4)-carbon in these three-membered vinyl heterocycles, as aziridines **9α-Ns** and **9β-Ns** and corresponding epoxides **1α** and **1β**, has never been observed.

18. It is worth noting that, compared with the corresponding aziridine conformers **9α'-Ns**:**9α"-Ns** ratio under neutral conditions, an increase of corresponding conformer **9α"-Ns-H**, with $-CH_2OBn$ side chain equatorial, is observed under acid conditions (from about 29% to about 46-50%) (Schemes 5 and 7 and Supplementary data, sections 4.2, 4.5 and 4.6) .

19. The carbaglycosylating ability of aziridine **9β-Ns** (60%, entry 2, Table 2) and epoxide

1α (57%, Scheme 1 and entry 2, Table 3), since obtained by *protocol B* reaction conditions (presence of only a small excess of nucleophile, 6 equiv), is more synthetically interesting than that obtained by *protocol A* (nucleophile as the solvent) with aziridine **9α-Ns** (62%, entry 1, Table 1) and epoxide **1β** (20%, Scheme 1 and entry 1, Table 4).

20. For the effect of ILs in favoring S_N1-type reaction pathways, see:
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21. The results obtained in the acid acetolysis of aziridine **9α-Ns** and in particular the presence of *syn-1,2-addition product* **24** (entries 4 and 5, Table 1) can be rationalized as previously admitted in order to justify the results and the presence of a corresponding *syn-1,2-addition product* in the acetolysis of epoxide **1α** (see ref. 9a).

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23. Epoxides **38**-**41** appeared as possibly effective carbaglycosyl donors for the preparation of 4-deoxy-4-(*N*-nosylamino)-5*a*-carba-D,L-glycosides, as previously found with other related oxirane systems. See: Bordoni V, Porkolab V, Sattin S, Thépaut M, Frau I, Favero L, Crotti P, Bernardi A, Fieschi F, Di Bussolo V. *RSC Adv.* 2016; 6 : 89578-89584.

24. An appropriate conformational study carried out on methoxy derivatives **20** and **27**, *anti-1,2-addition products* from aziridines **9α-Ns** and **9β-Ns**, respectively, has indicated that the corresponding conformers **20'** and **27'** with the side chain $–CH_2OBn$ equatorial are highly favored and practically the only conformers present at the equilibrium (nearly 98-99%, Schemes 13 and 14).