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Regio- and Stereoselectivity of the Addition of *O*-, *S*-, *N*-, and *C*-Nucleophiles to the *β* Vinyl Oxirane Derived from D-Glucal

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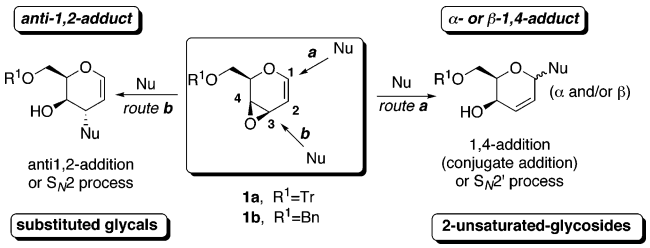
6-*O*-Trityl- (**1a**) and 6-(*O*-benzyl)-substituted epoxide (**1b**) derived from D-glucal were examined in their addition reactions with *O*-, *C*-, *N*-, and *S*-nucleophiles. A 1,4-regio- and *β*-stereoselective or an anti 1,2-addition pathway is commonly observed depending on the ability of the nucleophile to coordinate with the oxirane oxygen. When $TMSN_3$ or LiN_3 are used as azide-based nucleophiles, a 1,2-syn-addition pathway is also observed.

Introduction

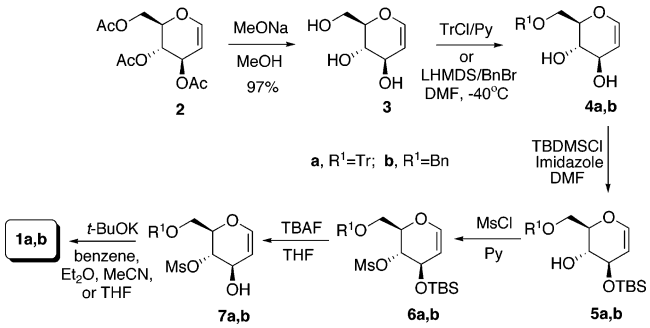
2-Unsaturated glycosides (pseudoglycals) are valuable synthetic intermediates, since the unsaturation can be further functionalized for the preparation of structural units present in many natural, biologically active compounds.[1]

In an attempt to devise a new method for the synthesis of substituted pseudoglycals, epoxides **1a**,**b** are at the same time glycals and vinyl oxiranes. As vinyl oxiranes, they are characterized by a double reactivity when subjected to a nucleophilic addition reaction: the nucleophile can attack (i) at the C(1) vinyl terminus of the "conjugate system" through a typical 1,4-addition pathway (conjugate addition or S_N2' process, route **a**) to yield α- and/or *β*-2-unsaturated glycosides (pseudoglycals), hereafter generically called α- and *β*-1,4-adducts, and (ii) at the allylic C(3) oxirane carbon to give substituted glycals through a direct, commonly completely anti 1,2-addition process (S_N2 process, *route* ***b***) to give substituted glycals, hereafter generically called anti-1,2-adducts (Scheme 1).[2] The C(1) of the vinyl oxirane system also corresponds to the classic reactive site of any glycal system, such as epoxides **1a**,**b** are. The regio- and stereochemical behavior of **1a** with *O*-nucleophiles (alcohols, phenol, and diacetone-D-glucose)[3a] and of **1b** with *C*-nucleophiles (Grignard reagents, dialkyllithium cuprates, and lithium alkyls)[3b] has been previously described. Further results obtained with *O*- and *C*-nucleophiles and new results obtained with *S*- and *N*-nucleophiles together with a comprehensive examination of the behavior of these vinyl oxiranes in nucleophilic addition reactions are now reported.

SCHEME 1



SCHEME 2



Results and Discussion

The synthesis of epoxides **1a**,**b** starts from the commercially available tri-*O*-acetyl-D-glucal (**2**) and proceeds through a simple protection−deprotection protocol, as shown in Scheme 2.[3]

Epoxides **1a** and **1b** are not sufficiently stable to be isolated, but they can be only prepared in situ by cyclization of the corresponding ultimate precursor, the hydroxy mesylate **7a** and **7b**, respectively, under alkaline conditions (*t*-BuOK) and then left to react immediately with a nucleophile (*O*-, *C*-, *N*-, and *S*-nucleophiles).

***O*-Nucleophiles.** The addition reaction of alcohols (MeOH, EtOH, *i*-PrOH, *t*-BuOH) to epoxide **1a** (alcohol

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(1) (a) Takhi, M.; Abdel-Rahman, A. A.-H.; Schmidt, R. R. *Synlett* **2001**, 427 and references therein. (b) Linde, R. G., II; Egbertson, M.; Coleman, R. S.; Jones, A. B.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 2771.

(2) Yamamoto, Y. In *Stereoselective Synthesis* (Houben-Weyl); Helmchem, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme Verlag: Stuttgart, 1996; Vol. 4, pp 2029−2040.

(3) (a) Di Bussolo, V.; Caselli, M.; Pineschi, M.; Crotti, P. *Org. Lett.* **2002**, *4*, 3695. (b) Di Bussolo, V.; Caselli, M.; Pineschi, M.; Crotti, P. *Org. Lett.* **2003**, *5*, 2173, and references therein.

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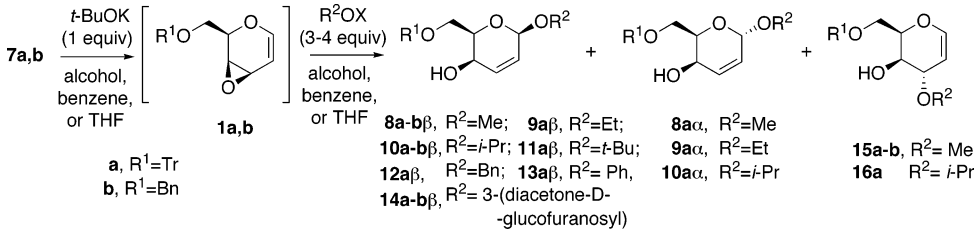
TABLE 1. Regio- and Stereoselectivity of the Addition Reaction of *O*-Nucleophiles to the in Situ Prepared Epoxides 1a and 1b



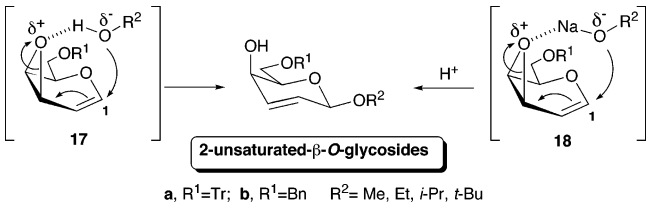
entry	epoxide	glycosyl acceptor (R^2OX) (protocol)[a]	solvent	time (h)	product(s)	yield (%)
1	**1a**	MeOH (A)	MeOH	0.5	**8a**β (50%)/**8a**α (50%)	90[b]
2	**1a**	EtOH (A)	EtOH	0.5	**9a**β (75%)/**9a**α (25%)	83[b]
3	**1a**	*i*-PrOH (A)	i-PrOH	0.5	**10a**β (95%)/ **10a**α (5%)	93[b]
4	**1a**	MeOH (B)	benzene	0.5	**8a**β	92[c]
5	**1a**	EtOH (B)	benzene	0.5	**9a**β	85[c]
6	**1a**	*i*-PrOH (B)	benzene	2	**10a**β	91[c]
7	**1a**	*t*-BuOH (B)	benzene	2	**11a**β	78[c]
8	**1a**	BnOH (B)	benzene	3	**12a**β	91[c]
9	**1a**	PhOH (B)	benzene	3	**13a**β	89[c]
10	**1a**	diacetone D-glucose (B)	benzene	2	**14a**β	76[c]
11	**1b**	MeOH (B)	benzene	18	**8b**β	69[c]
12	**1b**	*i*-PrOH (B)	benzene	1	**10b**β	64[c]
13	**1b**	diacetone D-glucose (B)	benzene	18	**14b**β	75[c]
14	**1a**	MeONa (B)	benzene	18	**8a**β	63[c]
15	**1b**	MeONa (B)	benzene	18	**8b**β	64[c]
16	**1a**	*i*-PrONa (B)	benzene	3	**10a**β	93[c]
17	**1a**	*i*-PrONa/15-Crown-5 (B)	benzene	18	**10a**β (60%)/**16a** (40%)	54[c]
18	**1b**	MeONa/15-Crown-5 (B)	THF	18	**8b**β (60%)/**15b** (40%)	49[c]
19	**1a**	$MeO^- Bu_4N^+$ (B)	THF	1	**15a**	97[b]
20	**1b**	$MeO^- Bu_4N^+$ (B)	THF	1	**15b**	92[b]

[a] A = protocol A: R^2OX as the solvent/nucleophile; B = protocol B: benzene or THF as the solvent, R^2OX,= 3−4 equiv. [b] Crude product. [c] After purification by flash chromatography.

used as the solvent/nucleophile, *protocol A*)[4] afforded the corresponding *O*-glycosides (1,4-adducts) in a completely 1,4-regioselective way, but with a stereoselectivity depending on the type of alcohol used.[3a] In fact, if in the reaction carried out in MeOH an almost 1:1 mixture of anomeric 2-unsaturated methyl α- and β-glycosides **8a**α and **8a**β was obtained, the use of more hindered alcohols such as EtOH and *i*-PrOH led to an increased C(1)-β-selectivity with a α/β ratio 25:75 and 5:95, respectively (entries 1−3, Table 1). Only when a reduced amount of alcohol (3 equiv) is added to the epoxide preformed in a benzene solution (*protocol B*)[4] is a completely 1,4-regio- and β-stereoselective process obtained with the exclusive formation of corresponding β-*O*-glycosides **8a**−**11a**β. Under these conditions, PhOH and BnOH could also be added in the same regio- and stereoselective fashion to afford β-*O*-glycosides **12a**β and **13a**β, respectively. In this way, a new β-stereoselective glycosylation procedure was found, which turned out to be useful also for the synthesis of a disaccharide (**14a**β) when diacetone-D-glucose was used as the glycosyl acceptor (entries 4−10, Table 1).[3a]

Control experiments now carried out, under protocol B, on epoxide **1b** in the reaction with MeOH, *i*-PrOH, and diacetone-D-glucose, as the glycosyl acceptors, afforded the corresponding β-*O*-glycosides **8b**β, **10b**β, and **14b**β in a completely regio- and stereoselective way,

SCHEME 3



indicating that the behavior of epoxide **1b** is practically identical to that of epoxide **1a** (entries 11−13, Table 1).[5]

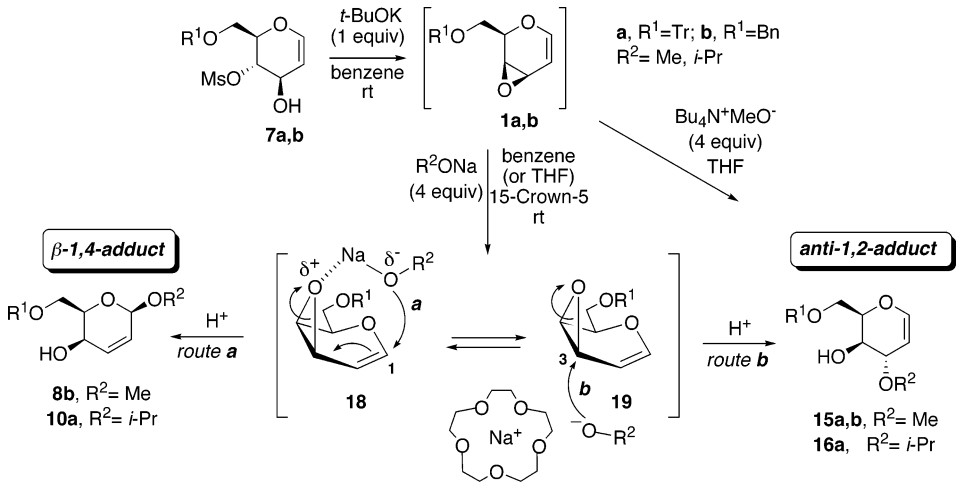
The regio- and stereochemical behavior of epoxides **1a**,**b** with *O*-nucleophiles was examined also with an alcoholate such as MeONa (**1a** and **1b**) and *i*-PrONa (**1a**) (protocol B).[4] Contrary to our expectations, according to which a complete 1,2-addition process appeared likely under these typical alkaline S_N2 conditions in the presence of a strong nucleophile, a complete 1,4-regio- and β-stereoselective process was observed, as in the case of alcohols (entries 14−16, Table 1).

The complete regio- and stereoselective result obtained in the addition reaction of *O*-nucleophiles (alcohols and alcoholates) to epoxides **1a** and **1b** can be rationalized by a coordination between the oxirane oxygen and the nucleophile through a hydrogen bond (alcohols) or the metal (alcoholates) as shown in structures **17** and **18**, respectively (Scheme 3). In this way, the nucleophile is efficiently transported on the β-face of the vinyl oxirane system and appropriately arranged for an entropically

(4) In the reactions carried out under *protocol A*, hydroxy mesylate **7a** (or **7b**) was treated with *t*-BuOK in the alcohol (MeOH, EtOH, *i*-PrOH, and *t*-BuOH) as the solvent. In the reactions carried out under *protocol B*, hydroxy mesylate **7a** (or **7b**) was treated with *t*-BuOK in anhydrous solvent (benzene, MeCN, Et_2O, THF); the nucleophile (3−4 equiv) was then added. In the reactions carried out under *protocol C*, hydroxy mesylate **7b** was treated with R^2MgBr (R^2 = Me, Ph, 3 equiv) in anhydrous Et_2O.

(5) For this reason, epoxides **1a** and **1b** were indifferently used in this work in order to study the behavior of this particular vinyl oxirane system in addition reactions with nucleophiles.

SCHEME 4



favored β-directed conjugate addition, as experimentally found. Confirmation of this rationalization was obtained in the reaction of epoxides **1b** and **1a** with MeONa and *i*-PrONa, respectively, in the presence of 15-crown-5, the crown ether specific for Na^+. In these modified reaction conditions, the corresponding β-1,4-adduct **8b**β and **10a**β was still present in the crude reaction mixture (nearly 60%), but a substantial amount of the corresponding anti 1,2-adduct, the hydroxy ether (HE) **15b** and **16a**, respectively, was also obtained (nearly 40%) (entries 17 and 18, Table 1 and Scheme 4). Evidently, as a consequence of the sequestering ability of the crown ether, under these conditions, the epoxide is not entirely coordinated with the nucleophile and an equilibrium exists between coordinated and noncoordinated epoxide molecules (structures **18** and **19**, respectively, Scheme 4). While in the former, the nucleophilic attack can effectively occur from the coordinated nucleophile to give the β-1,4-adduct (*route* ***a***), as stated above, the latter can react only with the free, noncoordinated nucleophile. In this case, the nucleophilic attack occurs necessarily at the C(3) allylic oxirane carbon (*route* ***b***), which, in the absence of any other factors, is the most reactive position in these vinyl oxirane systems,[6] and the corresponding 1,2-adduct (**15b** and **16a**) was obtained in a completely anti fashion in accordance with a classic S_N2-type oxirane ring-opening mechanism under the basic reaction conditions. These results indicate that in order to have a complete 1,2-addition pathway with *O*-nucleophiles, and probably also with other types of nucleophiles, in oxirane systems such as **1a** and **1b**, it is necessary to use a nucleophile which is not able to coordinate with the oxirane oxygen through a hydrogen bond or a counterion with a Lewis acid (LA) character. In this framework, we thought that tetrabutylammonium methoxide ($Bu_4N^+OMe^-$), a reagent not able to give a hydrogen bond and bearing a counterion (Bu_4N^+) with no LA properties, might be the appropriate reagent in order to have a complete 1,2-addition by the MeO^- species.[7]

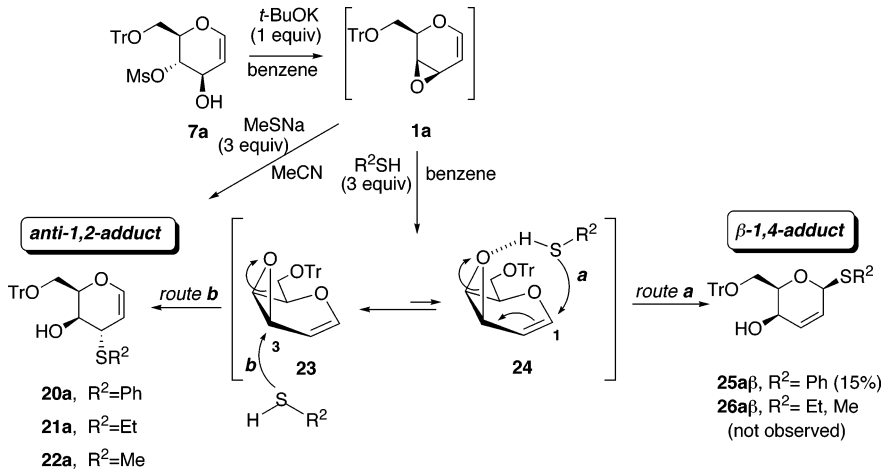
The reaction of epoxides **1a** and **1b** with $Bu_4N^+OMe^-$ (3 equiv, *protocol B*) in anhydrous THF resulted in a very clean reaction affording the corresponding, practically pure, anti 1,2-adduct, HE **15a** and **15b**, respectively, in a completely 1,2-regio- and anti stereoselective fashion (Scheme 4 and entries 19 and 20, Table 1). To date, this is the only protocol available in order to obtain this class of compounds.

S*-Nucleophiles.** Thiols such as PhSH and EtSH and a thiolate such as MeSNa were considered as typical *S*-nucleophiles. If compared with the corresponding reaction with alcohols, the addition reaction of PhSH and EtSH to epoxide **1a** (*protocol B*)[4] led to the obtainment of the corresponding anti-1,2-adduct (hydroxy thioethers **20a** and **21a**, respectively, Scheme 5) as largely the main (in the case of PhSH) or the sole reaction product (in the case of EtSH). Only in the case of PhSH, a slight, even if significant, amount (15%) of the corresponding β-1,4-adduct, the β-phenyl thioglycoside **25a**β, was observed. In the framework of the rationalization previously used for the corresponding reaction with alcohols, the reduced ability of thiols, with respect to alcohols, to coordinate with the oxirane oxygen considerably reduces the amount, in the reaction medium, of a coordinated species such as **24**, the only one which can lead to the β-1,4-adduct **25**−**26a**β (*route* ***a, Scheme 5), to the point that this type of addition is not experimentally observed with the less acidic EtSH ($pK_a = 10.78$) or observed only at a slight extent with the more acidic PhSH ($pK_a = 6.61$). As a consequence, under these conditions most of the epoxide is not coordinated with the nucleophile, and the reaction with the free thiol can occur only at the C(3) allylic oxirane carbon (*route* ***b***, Scheme 5), to yield the anti-1,2-adduct, as observed. Also with MeSNa a complete 1,2-anti addition pathway is observed with exclusive obtainment of the methylthio alcohol **22a**[3a] to indicate that the free, noncoordinated corresponding nucleophile should be involved under these reaction conditions.[8]

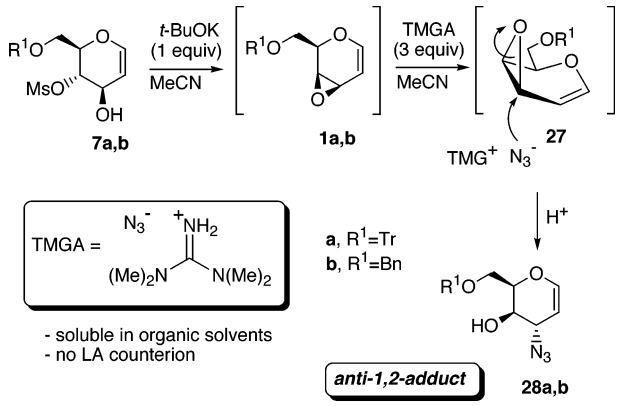
***N*-Nucleophiles.** Azide ion and diethylamine were taken as examples of *N*-nucleophiles. The reaction of epoxides **1a** with NaN_3 in MeCN led only to the recovery of the unreacted starting epoxide, due to the scarce solubility of the salt in the solvent. In the search for a source of azide ion soluble in an organic solvent, but

(6) Jaime, C.; Ortuño, R. M.; Font, J. *J. Org. Chem.* **1988**, *53*, 139.
(7) This new reagent ($Bu_4N^+OMe^-$) consists of the oily residue derived from the complete solvent evaporation of the commercially available 1 M $Bu_4N^+OH^-$ in MeOH: ^1H NMR δ 3.26 (s, 3H), 3.12−3.24 (m, 8H), 1.42−1.63 (m, 8H), 1.33 (sextet, 8H, $J = 7.2$ Hz), 0.87 (t, 12H, $J = 7.2$ Hz).

SCHEME 5



SCHEME 6



different from the common trimethylsilyl azide ($TMSN_3$, vide infra), tetramethylguanidinium azide (TMGA)[9] was thought to be appropriate and interesting to evaluate. TMGA is soluble in an organic solvent such as MeCN and, interestingly, is characterized by the presence of a counterion (tetramethylguanidinium, TMG^+) with no LA properties. The reaction of **1a** and **1b** with TMGA in MeCN (*protocol B*) proceeds in a completely 1,2-regio- and anti stereoselective way, affording the trans azido alcohol **28a** and **28b** (anti 1,2-adduct), respectively, as the only reaction product (Scheme 6).

As confirmation of previous considerations, the noncoordinating nature of the counterion (TMG^+) makes the epoxide react with the nucleophile (N_3^-) in a noncoordinated fashion, necessarily at the C(3) oxirane carbon, as shown in **27** (Scheme 6), affording the completely 1,2-regio- and anti stereoselective result.

The behavior of the more common organic source of N_3^-, $TMSN_3$, is decidedly different: the reaction of epoxide **1a** with $TMSN_3$ in anhydrous benzene (*protocol B*) turned out to be neither regio- nor stereoselective, and yielded a reaction mixture containing three addition products, the trans azido alcohol **28a** (anti 1,2-adduct), the 4-*O*-TMS derived β-azido glycoside **30a**β (β-1,4-adduct), and, surprisingly, the cis azido alcohol **29a** (syn 1,2-adduct) in a 16:45:39 ratio (^{1}H NMR) (Scheme 7).[10] The diastereoisomeric relationship between azido alcohols **28a** and **29a** was clearly established by appropriate decoupling and NOE experiments (^{1}H NMR) and was confirmed by their oxidation (PCC/CH_2Cl_2) to azido ketones **31a** and **32a**, respectively, whose diastereoisomeric relationship was determined as well (^{1}H NMR).

On the basis of the experience gained in the studies carried out on the stereoselectivity of the acid solvolysis of 2-aryloxiranes, an oxirane system in which substantial amounts of the corresponding syn adduct are commonly observed,[11] the results obtained in the reaction of **1a** with $TMSN_3$ can be rationalized by admitting the incursion in the reaction medium, after "protonation" of the oxirane oxygen by the TMS− group of the reagent, of two equilibrating intermediate species, **33** and **34** (Scheme 7). In the intimate ion/dipole pair **33**, in which the allylic C(3)−O oxirane bond is not yet broken, but only considerably extended, the nucleophilic attack can reasonably occur (*i*) at C(1) by the azido group coordinated to the oxirane oxygen through the TMS− group to give the β-1,4-adduct **30a**β (*route* ***a***) or (*ii*) at the allylic oxirane C(3) by a noncoordinated azido nucleophile to give the anti 1,2-adduct **28a** (*route* ***b***). Internal rearrangement of **33** with further loosening of the dipole (O-TMS−) from the allylic carbenium ion leads to the nucleophile separated ion/dipole pair **34**, in which the allylic oxirane bond is now completely broken and an extended coordination between the carbocationic center and the coordinated azido group is present. In **34**, the attack by the internal nucleophile with retention of configuration to give the cis azido alcohol **29a** (the syn 1,2-adduct, *route* ***c***) rather than by an external one with inversion of configuration (*route* ***d***), appears to be favored by entropic factors.[11] The

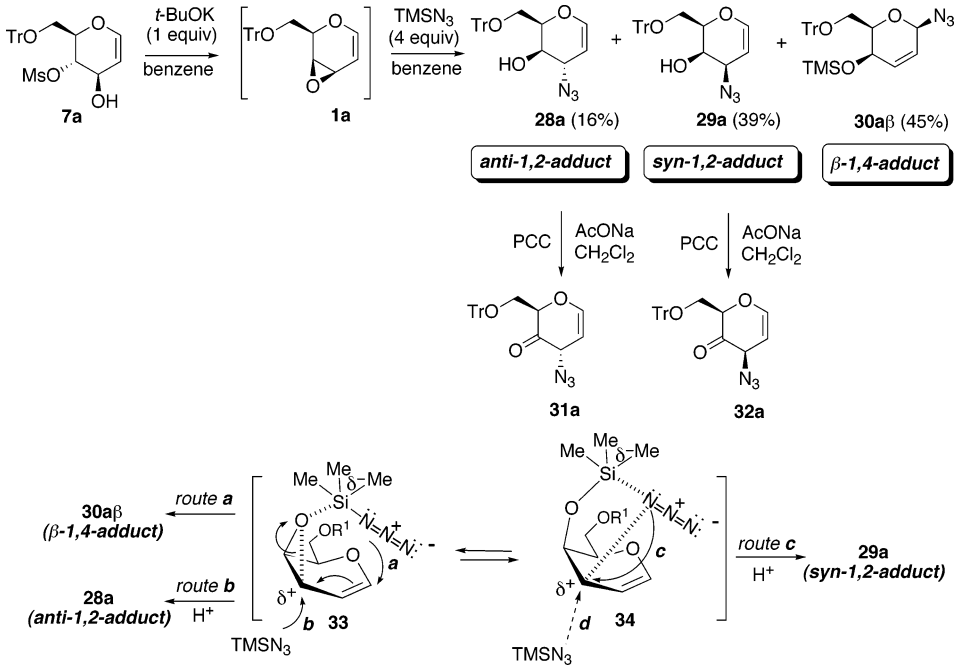
(8) It is interesting to note how the behavior of MeSNa (exclusive anti-1,2-addition) is different from the behavior of MeONa (exclusive β-1,4-addition) in the same reaction conditions. Probably, the different basicity of the corresponding nucleophilic species (MeS^- and MeO^-) and, as a consequence, the different nature of the associated ion/pair (MeS^-Na^+ and MeO^-Na^+) is responsible of the incursion (in the case of MeONa) or the absence (in the case of MeSNa) of the corresponding epoxide−nucleophile coordination through the metal to justify the opposite regiochemical behavior so far observed.

(9) (a) Crotti, P.; Di Bussolo, V.; Favero, L.; Macchia, F.; Pineschi, M. *Tetrahedron Lett.* **1996**, *37*, 1675. For the preparation of TMGA, see: Papa, A. J. *J. Org. Chem*. **1966**, *31*, 1426.

(10) Control experiments carried out on azido derivatives **28a**, **29a**, and **30a**β showed that they are stable under the reaction conditions ($TMSN_3$/benzene, rt).

(11) Crotti, P.; Dell'Omodarme, G.; Ferretti, M.; Macchia, F. *J. Am. Chem. Soc*. **1987**, *109*, 1463 and pertinent references therein.

SCHEME 7



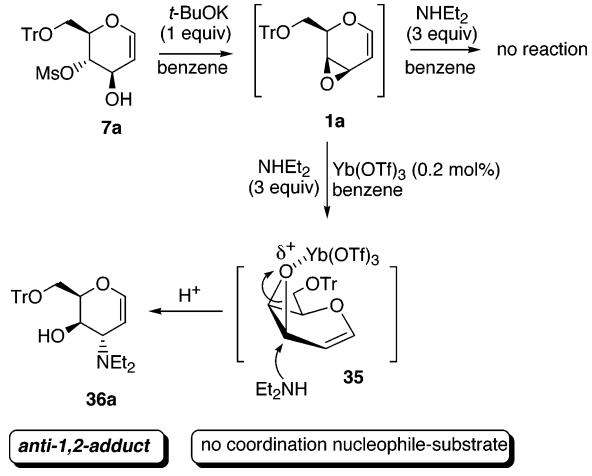
different nature of the "counterion" of the nucleophile (azido group) present in TMGA and $TMSN_3$ is clearly responsible for the completely different regio- and stereoselectivity obtained in the reaction of epoxide **1a** with these two N_3^--based nucleophiles.

In good agreement with the above-described results with TMGA and $TMSN_3$, the reaction of epoxide **1a** with LiN_3 in MeCN (*protocol B*) afforded a 7:3 mixture of cis azido alcohol **29a** (syn-1,2-adduct) and trans azido alcohol **28a** (anti-1,2-adduct). Evidently, the marked LA property of the counterion (Li^+) is able to polarize the C(3)−O oxirane bond and determine the incursion of a nucleophile separated ion/dipole pair, structurally corresponding to **34**, which leads to the syn adduct, the azido alcohol **29a**. Interestingly, when the more solvating THF is used, a mixture with an almost inverted composition (cis azido alcohol **29a**/trans azido alcohol **28a** = 20:80) was obtained.

The treatment of epoxide **1a** with $NHEt_2$ under *protocol B* did not afford any addition product. However, when $Yb(OTf)_3$, a previously described efficient catalyst for the addition reaction of amines to epoxides,[12] was added to the reaction mixture, a rapid reaction occurred with the exclusive formation of the corresponding anti 1,2-adduct, the trans amino alcohol **36a**. The absence of any coordination between the nucleophile (the amine) and the epoxide determines, as usual, a nucleophilic attack in a noncoordinated fashion on the allylic C(3) oxirane carbon under the necessary activation by the metal catalyst, as shown in structure **35** (Scheme 8).

***C*-Nucleophiles.** As for the reaction of epoxide **1b** with *C*-nucleophiles, different results were obtained depending on the type of reagent. Grignard reagents such as MeMgBr and PhMgBr did not react with epoxide **1b** generated in situ from hydroxy mesylate **7b** in the presence of *t*-BuOK (*protocol A*).[3b] However, when MeMgBr or PhMgBr were added directly to hydroxy mesylate **7b** (*protocol C*),[4] a clean reaction occurred with the formation of an almost 1:1 mixture of secondary alcohols **39b** and **40b** (R^2 = Me or Ph) (Scheme 9). Contrary to our previous report,[3b] in alcohols **39b** and **40b** a relative trans configuration is present between the two substituents at C(4) and C(5), as demonstrated by NOE experiments. This structural evidence would indicate that a highly stereocontrolled Grob fragmentation process on hydroxy mesylate **7b**, as shown in **37**, by the basic Grignard reagent (R^2MgBr) to the trans aldehyde **38**, then unstereoselectively attacked by the excess of R^2-MgBr, could more appropriately rationalize the result (Scheme 9).[13]

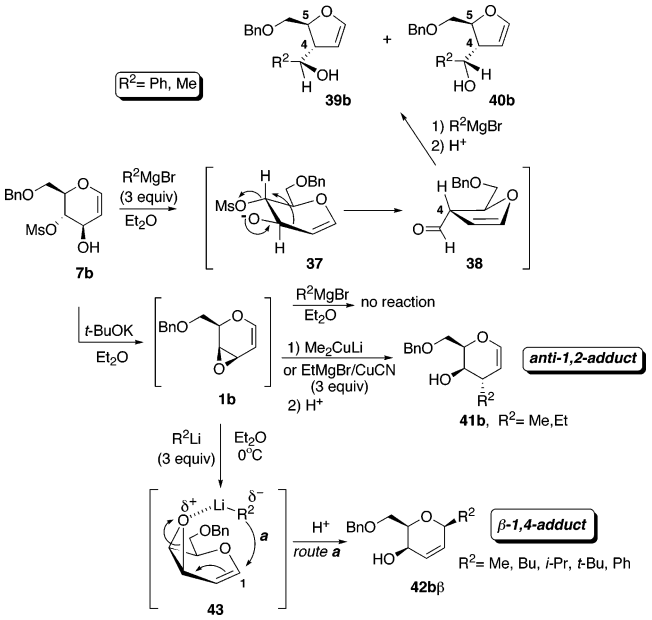
SCHEME 8



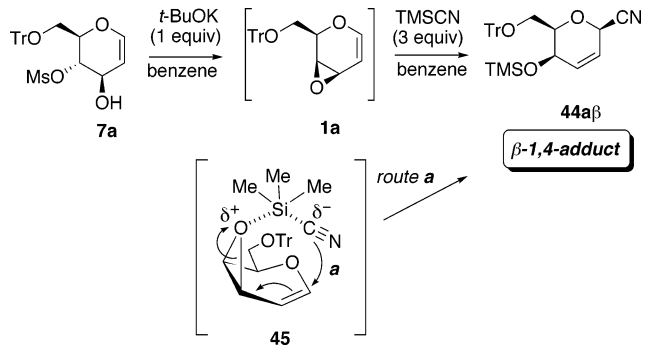
(12) Crotti, P.; Favero, L.; Macchia, F.; Pineschi, M. *Tetrahedron Lett*. **1994**, *35*, 7089.

(13) Initially, a highly stereocontrolled isomerization by the Grignard reagent (R^2MgBr) of the in situ formed epoxide **1b** to the C(4) epimer of aldehyde **38** (Scheme 9), then attacked by the excess of R^2MgBr, was thought to be responsible of the result and a cis configuration was consequently assigned to alcohols **39b** and **40b**.[3b] See also footnote 19 of ref 3b.

SCHEME 9



SCHEME 10

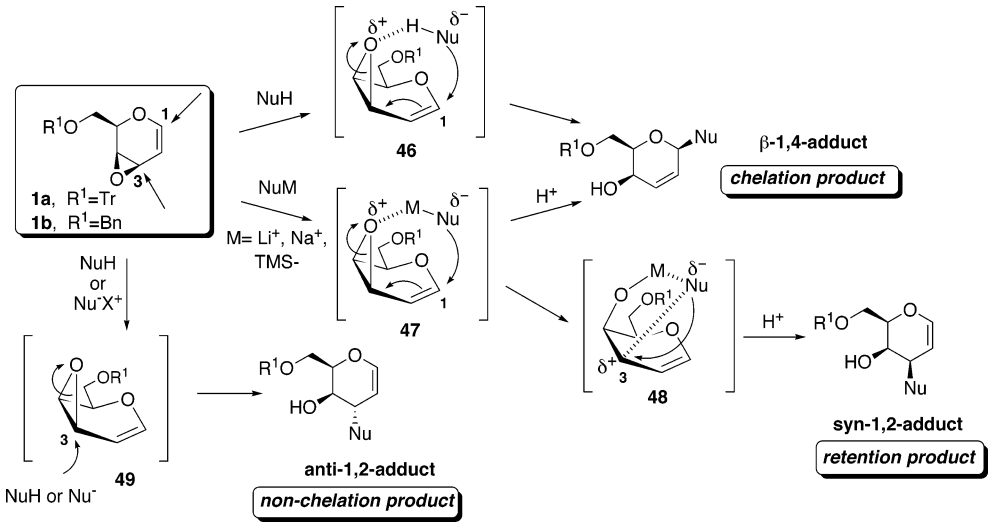


On their own, cuprates such as Me_2CuLi and EtMgBr in the presence of stoichiometric CuCN afforded only the corresponding 1,2-addition product, the alcohol **41b**, R^2 = Me, Et (Scheme 9).[3b] Only lithium alkyls such as MeLi, BuLi, *i*-PrLi, *t*-BuLi, and PhLi gave a completely 1,4-regio- and β-stereoselective result affording the corresponding β-*C*-glycosides **42b**β as the only reaction products. As previously, a coordination of the reagent (RLi) with the oxirane oxygen through the metal, as shown in **43**, was considered responsible for the observed regio- and stereoselectivity (Scheme 9).[3b]

As a further *C*-nucleophile, the cyanide species was examined. As in the case of NaN_3, the use of NaCN as a source of the cyanide ion was unsuccessful due to the scarce solubility of the salt in the reaction solvent (MeCN). On the contrary, the reaction of epoxide **1a** with TMSCN, a cyanide species soluble in an organic solvent such as MeCN (*protocol B*), afforded the corresponding β-*C*-glycoside, the nitrile **44a**β, as the only reaction product. Also this result is consistent with a coordination between the oxirane oxygen and the reagent through the TMS− group, as shown in structure **45** (Scheme 10), followed by a β-directed attack of the coordinated nucleophile on the C(1) of the vinyl oxirane system (*route* ***a***).

It is interesting to note the decidedly different behavior of the two silylated reagents utilized in the present study, $TMSN_3$ and TMSCN, in their reaction with epoxide **1a**. In the case of $TMSN_3$ a mixture of syn 1,2-, anti 1,2-, and β-1,4-adducts was obtained (Scheme 7), whereas with TMSCN the corresponding β-1,4-adduct was the only reaction product (Scheme 10). The different behavior of these two reagents should be ascribed to their different polarizability and, practically, to their different "acidity". In fact, as HN_3 (pK_a = 4.74) is more acidic than HCN (pK_a = 9.3), also $TMSN_3$ should reasonably be more "acidic" than TMSCN, and the −Si−N_3 bond more polarized than the corresponding −Si−CN bond. As a consequence, $TMSN_3$ is able to polarize the allylic oxirane C(3)−O bond until its rupture and to determine the formation of the allylic carbocation species **34** (Scheme 7), whose incursion is responsible, in particular, for the formation of the corresponding syn 1,2-adduct, otherwise difficult to be justified. With TMSCN, the coordination epoxide−nucleophilic reagent is not followed by a polarization of the allylic oxirane C(3)−O bond, and only the product, the β-1,4-adduct, deriving from the coordination process, is correctly observed (Scheme 10).

SCHEME 11



Conclusions

Taken as a whole, the results obtained in the addition reaction of *O*-, *N*-, *S*-, and *C*-nucleophiles to D-glucal derived epoxides **1a** and **1b**, allow us to make some general considerations about the behavior of these simple and interesting vinyl oxirane systems. In particular:

(*i*) When the nucleophile is able to coordinate with the oxirane oxygen of **1a**,**b**[14] through a hydrogen bond (ROH), a "protonation" process (TMSCN, $TMSN_3$) or a metal having LA properties (RONa, RLi), a nucleophilic attack by the coordinated nucleophile is highly favored and necessarily occurs, for structural reasons, only at the C(1) oxirane bond in a β direction (structures **46** and **47**, Scheme 11). The reaction is completely 1,4-regio- and β-stereoselective, affording the corresponding β-1,4-adduct, the "chelation product", as the only reaction product.

(*ii*) If the nucleophile coordinated with the oxirane oxygen is able, as in the case of $TMSN_3$ and LiN_3, to polarize the C(3)−O bond to the point of its complete rupture (structure **48**, Scheme 11), the formation of a syn 1,2-adduct, the "retention product", can be observed.

(*iii*) If the nucleophile is not able to coordinate with the oxirane oxygen of **1a**,**b**, the opening reaction pathway necessarily involves the free, noncoordinated epoxide with the free nucleophile. In this framework, the nucleophilic attack can occur only at the C(3) oxirane carbon which, in the absence of any other factors such as coordination, is the most reactive position in these glycal-derived oxirane systems (structure **49**, Scheme 11). The anti 1,2-adduct, the "nonchelation product", is, in this way, selectively and exclusively obtained.

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Supporting Information Available: General information and experimental details; spectral and analytical data of all compounds prepared in this study. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Obviously, the involvement in the coordination process of both the endocyclic and exocyclic oxygens present in **1a** and **1b** cannot be excluded.