Pergamon

Tetrahedron 58 (2002) 6069–6091

TETRAHEDRON

Regiochemical control of the ring opening of 1,2-epoxides by means of chelating processes. Part 17: Synthesis and opening reactions of *cis*- and *trans*-oxides derived from (2*S*,6*R*)-2-benzyloxy-6-methyl-3,6-dihydro-2*H*-pyran, (2*R*,6*R*)- and (2*S*,6*R*)-2-methoxy-6-methyl-5,6-dihydro-2*H*-pyran

Paolo Crotti,* Valeria Di Bussolo, Lucilla Favero, Franco Macchia and Mauro Pineschi

Dipartimento di Chimica Bioorganica e Biofarmacia, Università di Pisa, Via Bonanno 33, I-56126 Pisa, Italy

Received 24 February 2002; revised 15 May 2002; accepted 6 June 2002

Abstract—The regiochemical behavior of the title deoxy anhydrosugars, prepared in an enantioselective way starting from methyl α-D-glucopyranoside, was examined in opening reactions, both under standard and chelating conditions. The results clearly indicate the influence of the reaction conditions and the importance of the relative orientation of the methyl group with respect to the oxirane ring on the regiochemical outcome of these epoxides. An useful inversion of regioselectivity is obtained in some cases.

1. Introduction

Epoxides constitute a valuable synthetic tool for the construction of β-hydroxy-substituted functionalities by means of their opening reactions with a large variety of nucleophiles. While on the one hand the stereoselectivity of the opening process is, at least in the aliphatic and cycloaliphatic systems, under complete anti-stereocontrol, the regioselectivity depends on several electronic and conformational factors. We found that the presence of an *O*-functionality in a suitable position with respect to the oxirane ring and appropriate opening reaction conditions can direct the regioselectivity of the opening process by influencing the conformational equilibrium inside the reacting epoxide.[1]

Our interest in the chemistry of epoxides, particularly when applied to naturally occurring systems, recently led us to examine the chemical behavior of the diastereoisomeric deoxy anhydrosugars **1** and **2**, thus obtaining some preliminary information about the chemical behavior of this class of compounds.[2] In view of the importance of these oxirane systems for the construction of derivatized branched anhydrosugars, we synthesized the chiral, non-racemic, deoxy anhydropyranosides **3**–**8**, a sort of branched sugars, like **1** and **2**, because of the presence of a methyl as the C(5)-substituent, and examined their stereo- and regiochemical behavior in opening reactions with nucleophiles. Enantiomeric methyl glycosides of epoxides **1**–**4** were previously synthesized and the corresponding regiochemical behavior examined in nucleophilic opening reactions carried out only under standard not chelating reaction conditions.[3,4] As a consequence, a more detailed examination of the regiochemical behavior of the oxirane system corresponding to epoxides **1**–**4**, also including opening reactions carried out under chelating conditions, appeared to us deserving of consideration.[4]

Diastereoisomeric epoxides *cis*,*trans*-**3** and *trans*,*cis*-**4**,[5] formally derived from (2*S*,6*R*)-2-benzyloxy-6-methyl-3,6-dihydro-2*H*-pyran (**9**), are regioisomers of the diastereoisomeric epoxides **5**–**8**, formally derived from (2*R*,6*R*)-(**10**) (epoxides *cis*,*cis*-**5** and *trans*,*trans*-**6**) and (2*S*,6*R*)-2-methoxy-6-methyl-5,6-dihydro-2*H*-pyran (**11**) (epoxides *cis*,*trans*-**7** and *trans*,*cis*-**8**). Epoxides **3** and **4** are diastereoisomers of the previously studied epoxides *cis*,*cis*-**1** and *trans*,*trans*-**2**. The choice of methyl glycosides in the case of epoxides **5**–**8**, unlike the benzyl glycosides utilized in the case of epoxides **3** and **4**, and in the previously studied epoxides **1** and **2** was simply based on the easy availability of the non-racemic starting material (vide infra) necessary for their preparation.[6]

2. Results

Glycal (−)-**17**, the advanced precursor for the synthesis of both epoxides **3** and **4**, was prepared from the commercially

Keywords: deoxy anhydrosugars; epoxides; regioselectivity; opening reactions.

* Corresponding author. Tel.: +39-050-44074; fax: +39-050-43321; e-mail: crotti@farm.unipi.it

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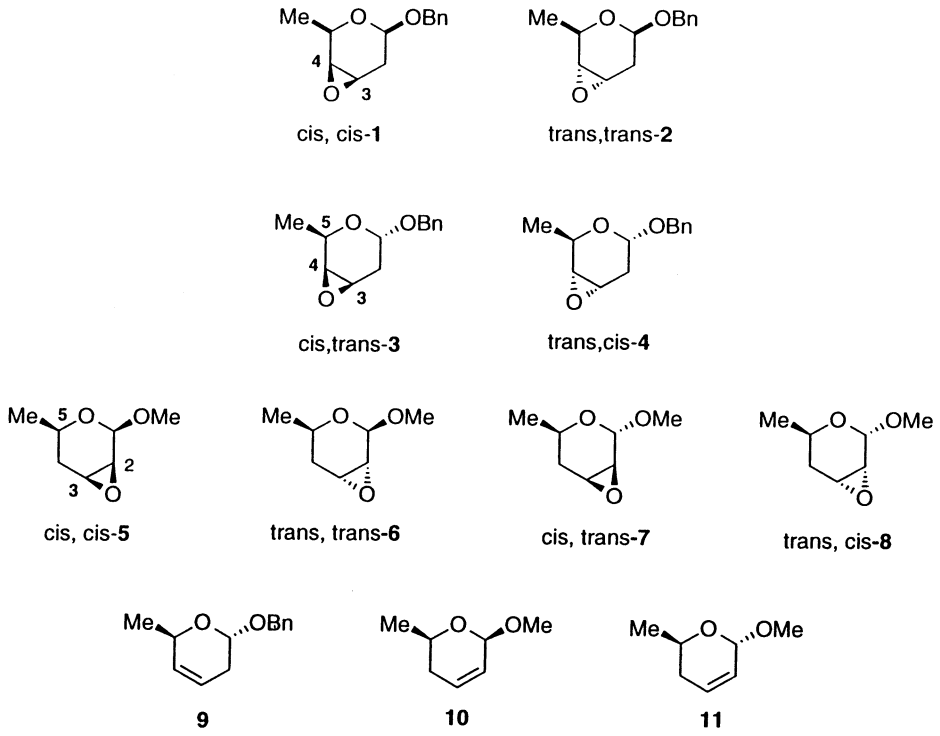
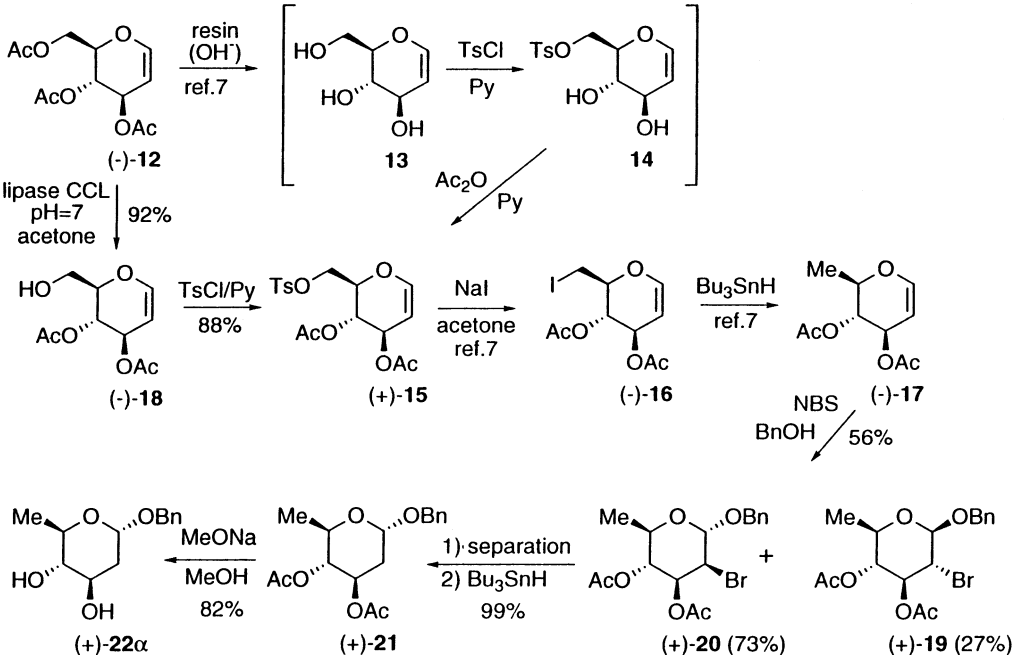


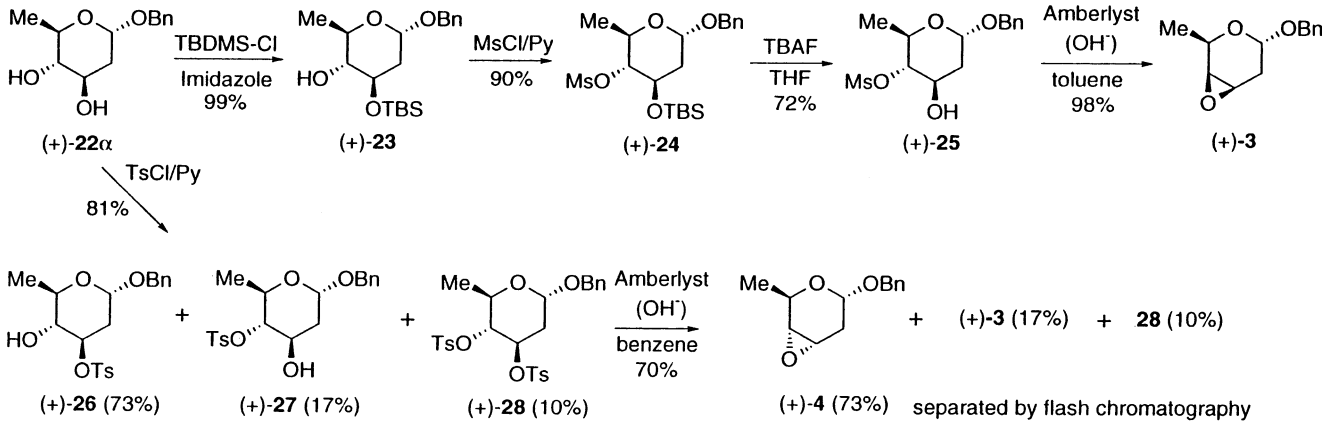
available tri-(*O*-acetyl)-D-glucal [(−)-**12**], in accordance with a previously described procedure through the triol **13**, the monotosylate **14**, the diacetate (+)-**15** and the iodide (−)-**16**, as shown in Scheme 1.[7] Because of the lengthiness of this procedure, we envisaged a more direct approach to diacetate (+)-**15**, consisting of an initial selective hydrolysis of glucal (−)-**12** by lipase CCL to give the primary alcohol (−)-**18**, then transformed into (+)-**15**, by the TsCl/Py protocol.

The reaction of (−)-**17** with NBS in the presence of benzyl alcohol[8] afforded a 27:73 mixture of α- and β-benzyl glycosides (+)-**19** and (+)-**20**. α-Glycoside (+)-**20** was separated and dehalogenated with Bu_3SnH to give the α-glycoside (+)-**21** which was hydrolyzed (MeONa/MeOH) to the desired diol (+)-**22**α, the ultimate precursor of epoxides **3** and **4** (Scheme 1).

The consistently different steric hindrance of the secondary hydroxyl functionalities present in diol (+)-**22**α allowed a stereoselective synthesis of epoxide **3** (Scheme 2). In fact, the reaction of (+)-**22**α with TBDMS-Cl (1 equiv.) in DMF



Scheme 1.

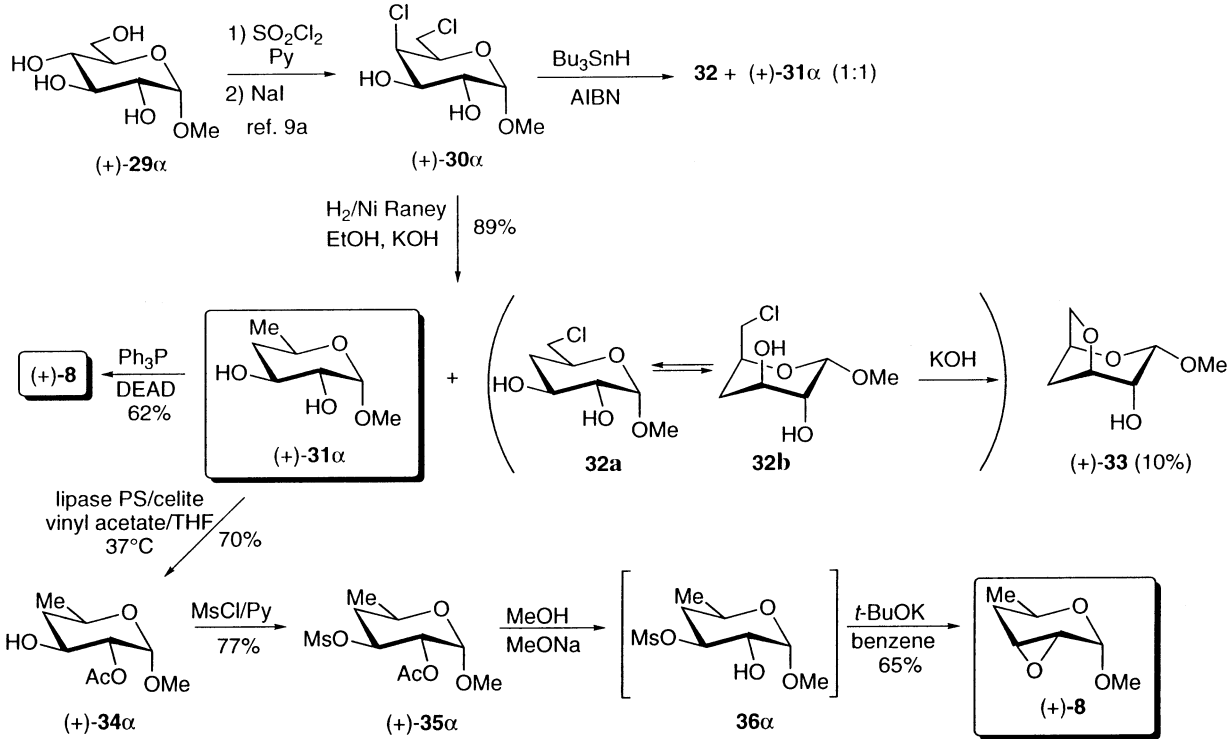


Scheme 2.

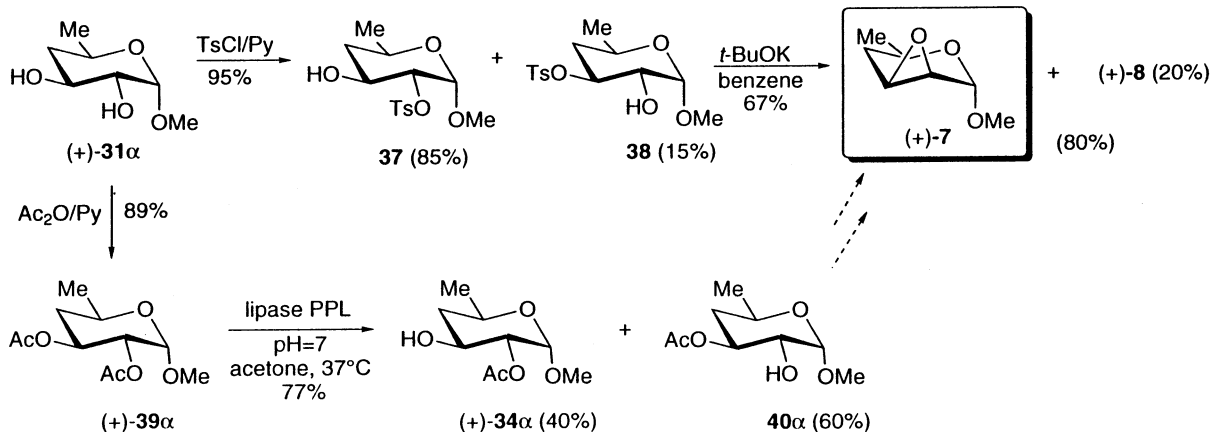
led only to the mono C(3)-*O*-TBS protected derivative (+)-**23**, subsequently transformed into the mesylate (+)-**24**. Deprotection of (+)-**24** by TBAF afforded the *trans* hydroxy mesylate (+)-**25** which was subjected to base-catalyzed cyclization to give epoxide (+)-**3**. On the other hand, epoxide (+)-**4** was obtained only by the monotosylation of diol (+)-**22**α, giving a 73:17 mixture of monotosylates (+)-**26** and (+)-**27**, accompanied by a small amount of ditosylate (+)-**28** (10%), which were directly cyclized (basic Amberlyst) to a corresponding mixture of epoxides (+)-**4** and (+)-**3**. Separation of this mixture by flash chromatography afforded pure epoxide (+)-**4** (Scheme 2).

The diol (+)-**31**α necessary for the synthesis of epoxides **7** and **8** was prepared starting from commercially available methyl α-D-glucopyranoside [(+)-**29**α]. Following a previously described procedure,[9a] treatment of (+)-**29**α with SO_2Cl_2, followed by reaction of the intermediate dichlorosulfate with catalytic NaI, afforded the dichloro diol (+)-**30**α which was dehalogenated (H_2/Ni-Raney/KOH) to the desired 2,3-diol (+)-**31**α.[9,10] Actually, in the dehalogenation process of (+)-**30**α, a certain amount of the dioxabicyclic compound (+)-**33** (10%) was obtained. Compound (+)-**33** reasonably arises from the monochloro diol **32**, the reaction intermediate deriving from a faster hydrogenolysis rate of the secondary C(4)–Cl bond of (+)-**30**α, which can in part intramolecularly cyclize, in alkaline reaction conditions through its diaxial conformer **32b**, to (+)-**33**. Compound (+)-**33** can be separated from (+)-**31**α by flash chromatography (Scheme 3).

Diol (+)-**31**α was transformed in a completely regioselective way into the monoacetate (+)-**34**α by means of



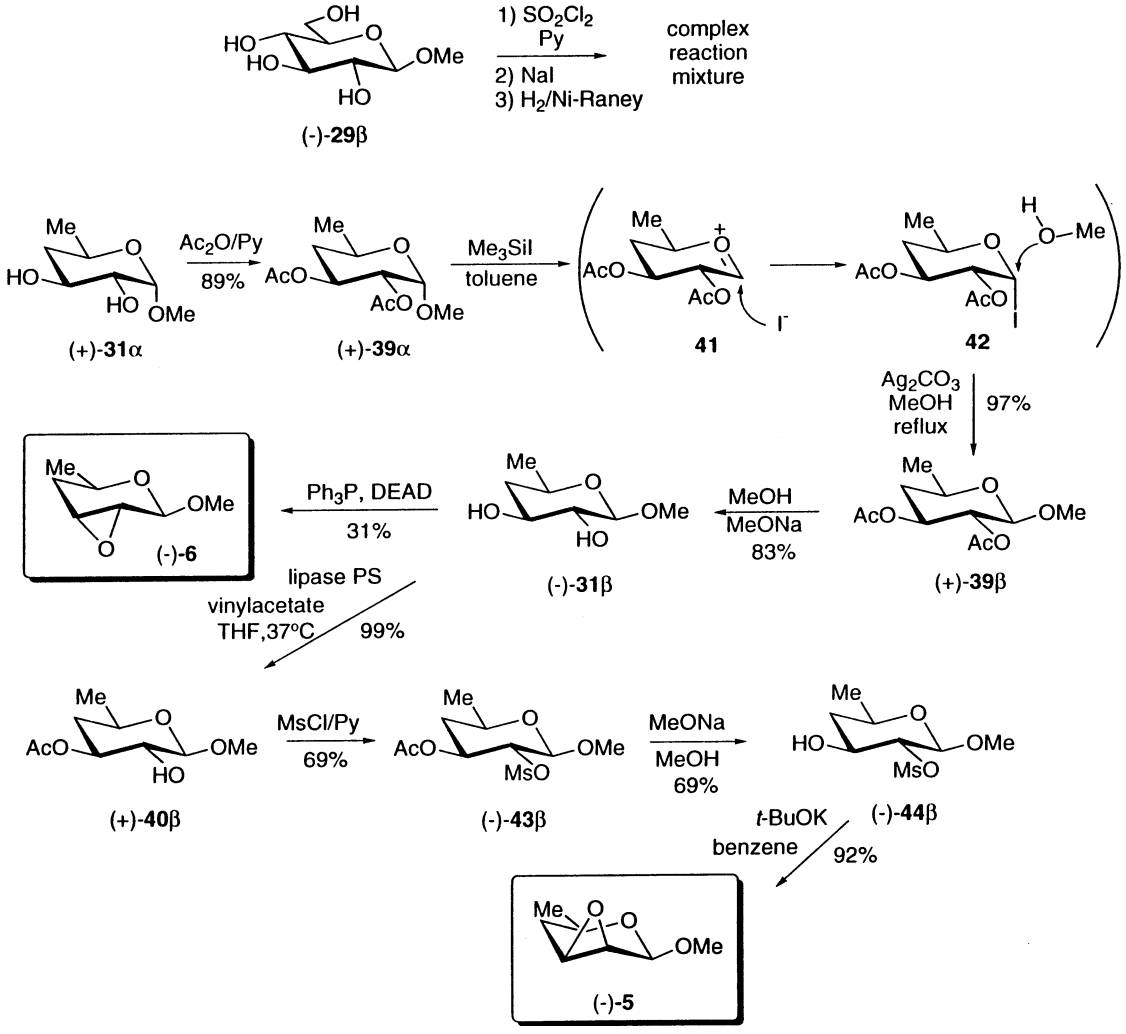
Scheme 3.



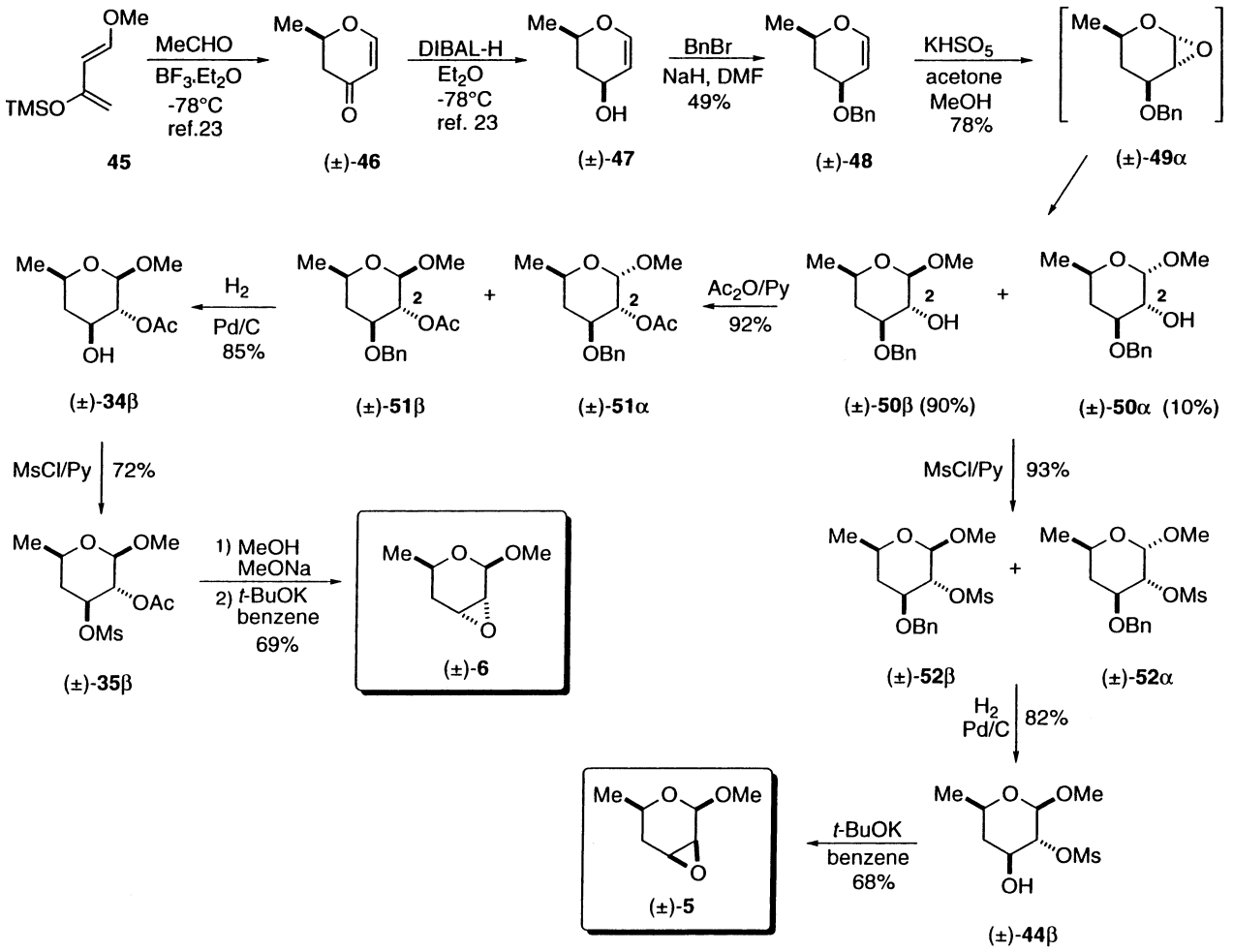
Scheme 4.

a transesterification process catalyzed by lipase PS. Treatment of (+)-**34**α with MsCl/Py afforded the acetoxy mesylate (+)-**35**α, subsequently hydrolyzed to the intermediate hydroxy mesylate **36**α which was not separated but directly cyclized under alkaline conditions to epoxide (+)-**8**.[11] Epoxide (+)-**8** can also be prepared in a straightforward, completely stereoselective way with a satisfactory yield (62%) by application of the Mitsunobu reaction protocol (PPh_3-DEAD)[12] to diol (+)-**31**α, indicating an initial completely regioselective reactivity of the C(3)–OH in these conditions (Scheme 3).

No selective synthesis was envisaged for epoxide (+)-**7** which was prepared only by monotosylation of diol



Scheme 5.



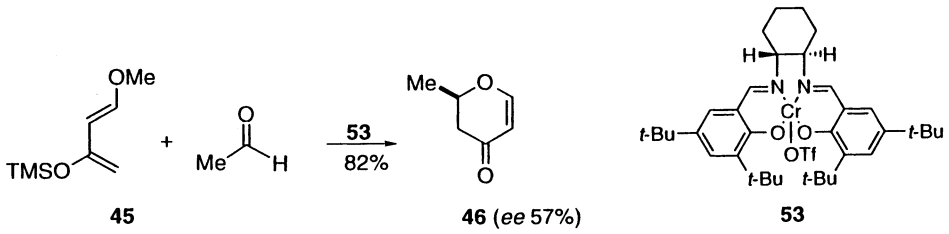
Scheme 6.

(+)-**31**α, giving an 85:15 mixture of tosylates **37** and **38** which were not separated, but directly cyclized to a corresponding mixture of epoxides (+)-**7** and (+)-**8**, from which epoxide (+)-**7**[9d,11] was obtained pure by flash chromatography (Scheme 4).[13]

For the synthesis of diastereoisomeric epoxides (−)-**5** and (−)-**6**, we needed diol (−)-**31**β. We initially thought of applying to the commercially available methyl-β-D-glucopyranoside [(−)-**29**β] the same protocol previously employed with anomer (+)-**29**α for the synthesis of diol (+)-**31**α. Unfortunately, the initial reaction of (−)-**29**β with SO_2Cl_2 followed by reduction with NaI and hydrogenolysis afforded only a complex reaction mixture containing the desired diol (−)-**31**β in a decidedly unsatisfactory yield (10%, ^{1}H NMR) (Scheme 5).[14]

The problem of the synthesis of these epoxides was effectively solved by applying to diacetate (+)-**39**α[16a] (obtained by acetylation of (+)-**31**α) a modification of a procedure previously utilized for the β-glycosidation of similar substrates.[17] In this way, the reaction of diacetate (+)-**39**α with Me_3SiI, followed by treatment with MeOH in the presence of Ag_2CO_3, led to the anomeric diacetate (+)-**39**β,[16b] in a completely stereoselective way. This result is rationalized by admitting the initial intermediate formation of carboxonium ion **41**, selectively attacked by the nucleophile (I^-) on the less hindered α-face (axial attack) to give the α-iodide **42**.[18] Subsequent S_N2 displacement by MeOH affords diacetate (+)-**39**β, as observed (Scheme 5). Diacetate (+)-**39**β is then hydrolyzed to the desired 2,3-diol (−)-**31**β[19] which constitutes the effective advanced synthetic intermediate for the synthesis of epoxides **5** and **6**. Transacetylation of (−)-**31**β catalyzed by lipase PS afforded regioselectively the monoacetate (+)-**40**β,[20] which was transformed into mesylate (−)-**43**β, and then hydrolyzed to the hydroxy mesylate (−)-**44**β. Subsequent cyclization of (−)-**44**β under alkaline conditions afforded epoxide (−)-**5** (Scheme 5).[21]

The reaction of diol (−)-**31**β under Mitsunobu operating conditions proceeds, as in the corresponding α-system, with initial completely selective reactivity of the C(3)–OH[22] to give epoxide (−)-**6**,[21] as the only reaction product. As a consequence, it was possible, in this system, to proceed to the synthesis of both epoxides (−)-**5** and (−)-**6** in a completely stereoselective fashion. Moreover, it is to be noted that both couples of diastereoisomeric epoxides **5**–**8** may be synthesized starting from a single precursor, the 2,3-diol (+)-**31**α, easily obtained from a commercially available and cheap starting material, such as methyl α-D-glucopyranoside [(+)-**29**α].



Scheme 7.

As for the β-system represented by epoxides **5** and **6**, we had initially envisaged also a non-enantioselective (racemic) synthetic procedure, with the possibility of transforming it into an enantioselective one, utilizing an asymmetrical approach in the synthetic step in which the first stereogenic centre is introduced (vide infra).[23] The racemic synthetic sequence utilizes glycal (±)-**48** which was obtained by benzylation (BnBr/NaH) of alcohol (±)-**47**, prepared as previously described.[23] Oxidation of (±)-**48** with dimethyl dioxirane (DMDO) generated in situ (oxone®–MeOH–acetone) leads to the intermediate, unseparated epoxide (±)-**49**α, which undergoes an opening reaction with the MeOH present in the reaction mixture to give a 9:1 mixture of the two anomeric methyl glycosides (±)-**50**β and (±)-**50**α, subsequently transformed by acetylation into a corresponding mixture of acetates (±)-**51**β and (±)-**51**α. The ^{1}H NMR spectra of the mixture of (±)-**51**α and (±)-**51**β show that these two compounds have the same configuration at C(2) (a *gluco* configuration), thus indicating that the corresponding methyl glycosides (±)-**50**α and (±)-**50**β are really opening products of the same intermediate epoxide (±)-**49**α, the former being the product of retention and the latter the product of inversion (Scheme 6).[24]

The 9:1 mixture of benzyloxy acetates (±)-**51**β and (±)-**51**α was deprotected by hydrogenolysis to give only hydroxy acetate (±)-**34**β which was transformed into mesylate (±)-**35**β. Alkaline hydrolysis of (±)-**35**β (MeONa/MeOH) followed by cyclization with *t*-BuOK in anhydrous benzene afforded pure epoxide (±)-**6**. On the

Table 1. Regioselectivity of the ring opening reactions of epoxides **1**, **3**, **5**, and **7**

Entry	Epoxide	Reagents	Solvent	Reaction conditions (°C)[a]	Reaction time	*C-2* or *C-4 product*	*C-3 product*	Yield (%)
1	**1**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	18 h	<1[b,c,d]	>99	95
2		$NaN_3/LiClO_4$	MeCN	B (80)	18 h	<1[b,c]	>99	97
3	**1**	MeONa	MeOH	A (80)	4 h	<1[b,c,d]	>99	99
4		$MeOH/H_2SO_4$	MeOH	A (rt)	1 h	<1[b,c]	>99	33
5		$MeOH/LiClO_4$	MeOH	B (80)	18 h	complex mixture[c]		
6	**1**	Et_2NH	EtOH	A (80)	7 days	<1[b,c,d]	>99	94
7		$Et_2NH/LiClO_4$	MeCN	B (80)	18 h	<1[b,c]	>99	95
8	**1**	$PhSH/NEt_3$	MeOH	A (rt)	18 h	<1[b,c]	>99[c]	95
9		$PhSH/LiClO_4$	MeCN	B (80)	18 h	complex mixture		99
10	**3**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	18 h	7[b,d]	93	97
11		$NaN_3/LiClO_4$	MeCN	B (80)	18 h	5[b]	95	99
12	**3**	MeONa	MeOH	A (80)	24 h	21[b,d]	79	87
13		$MeOH/LiClO_4$	MeOH	B (80)	24 h	<1[b]	>99	30
14	**3**	Et_2NH	EtOH	A (80)	30 h	<1[b,d]	>99	97
15		$Et_2NH/LiClO_4$	MeCN	B (80)	18 h	<1[b]	>99	95
16	**3**	$PhSH/NEt_3$	MeOH	A (rt)	18 h	7[b]	93	99
17		$PhSH/LiClO_4$	MeCN	B (80)	3 days	complex mixture		
18	**5**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	24 h	<1[e]	>99	97
19		$NaN_3/LiClO_4$	MeCN	B (80)	24 h	<1[e]	>99	80
20	**5**	MeONa	MeOH	A (80)	1 h	<1[e]	>99	70
21		$MeOH/LiClO_4$	MeOH	B (80)	24 h	<1[e]	>99	35
22	**5**	Et_2NH	EtOH	A (80)	5 days	<1[e]	>99	84
23		$Et_2NH/LiClO_4$	MeCN	B (80)	18 h	<1[e]	>99	92
24	**5**	$PhSH/NEt_3$	MeOH	A (rt)	18 h	<1[e]	>99	99
25		$PhSH/LiClO_4$	MeCN	B (80)	24 h	<1[e]	>99	99
26	**7**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	18 h	<1[e]	>99	99
27		$NaN_3/LiClO_4$	MeCN	B (80)	18 h	<1[e]	>99	88
28	**7**	MeONa	MeOH	A (80)	3 h	<1[e]	>99	99
29		$MeOH/LiClO_4$	MeOH	B (80)	18 h	<1[e]	>99	39
30	**7**	Et_2NH	EtOH	A (80)	2 days	<1[e]	>99	99
31		$Et_2NH/LiClO_4$	MeCN	B (80)	2 h	<1[e]	>99	99
32	**7**	$PhSH/NEt_3$	MeOH	A (rt)	24 h	<1[e]	>99	99
33		$PhSH/LiClO_4$	MeCN	B (80)	24 h	<1[e]	>99	86

[a] A: standard reaction conditions; B: chelating reaction conditions, Ref. 4.
[b] ***C-4 product***.
[c] Ref. 2.
[d] For the related results obtained with the corresponding enantiomeric methyl glycosides, see Ref. 3.
[e] ***C-2 product***.

Table 2. Regioselectivity of the ring opening reactions of epoxides **2**, **4**, **6** and **8**

Entry	Epoxide	Reagents	Solvent	Reaction conditions (°C)[a]	Reaction time	*C-2* or *C-4 product*	*C-3 product*	Yield (%)
1	**2**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	18 h	69[b,c,d]	31	94
2		$NaN_3/LiClO_4$	MeCN	B (80)	18 h	35[b,c]	65	95
3		$NaN_3/LiClO_4$	MeOH	B (80)	18 h	18[b,c]	82	95
4	**2**	$MeOH/H_2SO_4$	MeOH	A (rt)	1 h	59[b,c]	41	41
5		MeONa	MeOH	A (80)	24 h	21[b,c,d]	79	83
6		$MeOH/LiClO_4$	MeOH	B (80)	24 h	complex mixture[c]		
7	**2**	Et_2NH	EtOH	A (80)	30 h	45[b,c,d]	55	60
8		$Et_2NH/LiClO_4$	MeCN	B (80)	18 h	15[b,c]	85	96
9	**2**	$PhSH/NEt_3$	MeOH	A (rt)	18 h	65[b,c]	35	94
10		$PhSNa/LiClO_4$	MeCN	B (80)	3 days	50[b,c]	50	75
11	**4**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	18 h	13[b,d]	87	99
12		$NaN_3/LiClO_4$	MeCN	B (80)	18 h	76[b]	24	99
13	**4**	MeONa	MeOH	A (80)	4 h	4[b,d]	96	99
14		$MeOH/H_2SO_4$	MeOH	A (rt)	1 h	complex mixture		
15		$MeOH/LiClO_4$	MeOH	B (80)	18 h	90[b]	10	87
16		$MeOH/LiClO_4$	MeCN	B (80)	18 h	66[b]	34	23
17	**4**	Et_2NH	EtOH	A (80)	7 days	15[b,d]	85	52
18		$Et_2NH/LiClO_4$	MeCN	B (80)	18 h	46[b]	54	99
19	**4**	$PhSH/NEt_3$	MeOH	A (rt)	18 h	5[b]	95	99
20		$PhSH/LiClO_4$	MeCN	B (80)	18 h	55[b]	45	99
21	**6**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	24 h	33[e]	67	92
22		$NaN_3/LiClO_4$	MeCN	B (80)	24 h	37[e]	63	45
23	**6**	MeONa	MeOH	A (80)	1 h	38[e]	62	97
24		$MeOH/LiClO_4$	MeOH	B (80)	18 h	complex mixture		
25	**6**	Et_2NH	EtOH	A (80)	4 days	33[e]	67	79
26		$Et_2NH/LiClO_4$	MeCN	B (80)	18 h	32[e]	68	10
27	**6**	$PhSH/NEt_3$	MeOH	A (rt)	24 h	34[e]	66	99
28		$PhSH/LiClO_4$	MeCN	B (80)	24 h	49[e]	51	11
29	**8**	NaN_3/NH_4Cl	$MeOH/H_2O$	A (80)	18 h	23[e]	77	90
30		$NaN_3/LiClO_4$	MeCN	B (80)	18 h	18[e]	82	86
31	**8**	MeONa	MeOH	A (80)	4 h	30[e]	70	95
32		$MeOH/LiClO_4$	MeOH	B (80)	18 h	3[e]	97	50
33	**8**	Et_2NH	EtOH	A (80)	8 days	16[e]	84	80
34		$Et_2NH/LiClO_4$	MeCN	B (80)	5 h	30[e]	70	35
35	**8**	$PhSH/NEt_3$	MeOH	A (rt)	18 h	33[e]	67	98
36		$PhSH/LiClO_4$	MeCN	B (80)	18 h	67[e]	33	93

[a] A: Standard reaction conditions; B: Chelating reaction conditions, Ref. 4.
[b] ***C-4 product***.
[c] Ref. 2.
[d] For the related results obtained with the corresponding enantiomeric methyl glycosides, see Ref. 3.
[e] ***C-2 product***.

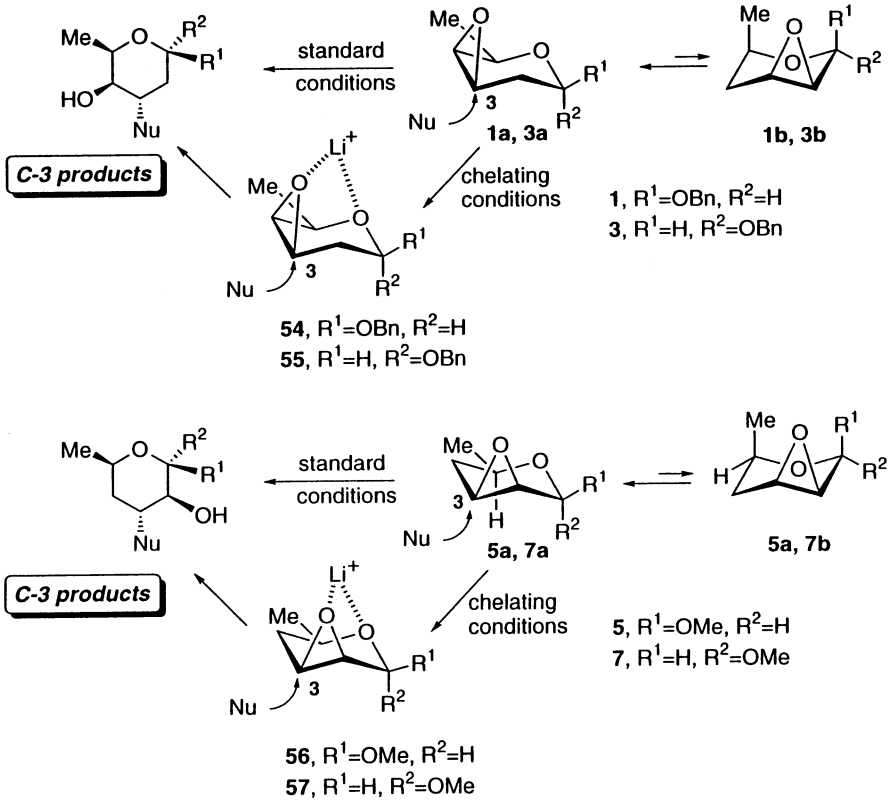
other hand the 9:1 mixture of hydroxy ethers (±)-**50**β and (±)-**50**α can be utilized for the synthesis of diastereoisomeric epoxide (±)-**5**. In fact, the treatment of this mixture with MsCl afforded a corresponding mixture of mesylates (±)-**52**β and (±)-**52**α which were deprotected by hydrogenolysis to give the hydroxy mesylate (±)-**44**β as the only reaction product. Cyclization of (±)-**44**β under alkaline conditions afforded pure racemic epoxide **5** (Scheme 6).

As anticipated earlier, in order to transform the racemic process described above into an enantioselective one, the initial cycloaddition reaction between Danishefsky diene and acetaldehyde was repeated in the presence of (*R*,*R*)(salen)Cr(III)OTf complex (**53**).[25a] Contrary to expectations based on previous corresponding results,[25b] the cycloadduct, the dihydropyranone **46**, was obtained only with 57% ee. Attempts to increase the ee of the process were unsuccessful (Scheme 7).

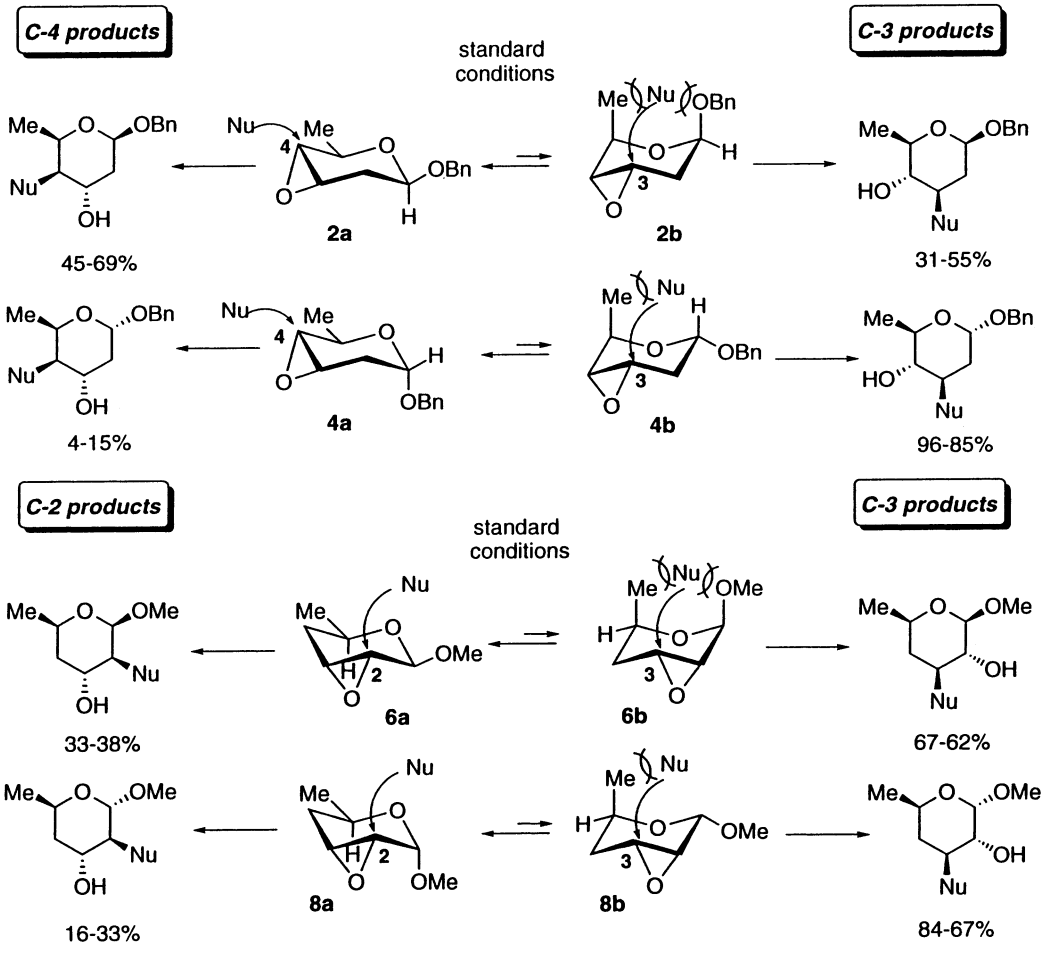
3. Discussion

Epoxides **3**–**8** were subjected to ring opening reactions with some representative nucleophiles both under standard and chelating conditions.[4] The results obtained are shown in Tables 1 and 2, where for comparison also the results previously obtained with epoxides **1** and **2** are reported, too.[2] The regiochemical results obtained with epoxides **1**–**4** under standard conditions (MeONa/MeOH, NaN_3/NH_4Cl, $NHEt_2$/EtOH) are quite similar to the ones previously obtained with the corresponding enantiomeric methyl glycosides.[3] The results indicate that the regioselectivity with epoxides **3**–**8**, and with the previously studied epoxides **1** and **2**,[2] is strongly influenced by the electron-withdrawing inductive effect of the nearby acetal functionality, and that the sensitivity of epoxides **1**–**8** to different operating conditions (standard or chelating) is closely linked to the structure and particularly to the relationship between the oxirane moiety and the branched chain (the methyl group), and to the distance of the oxirane ring from the acetal group.

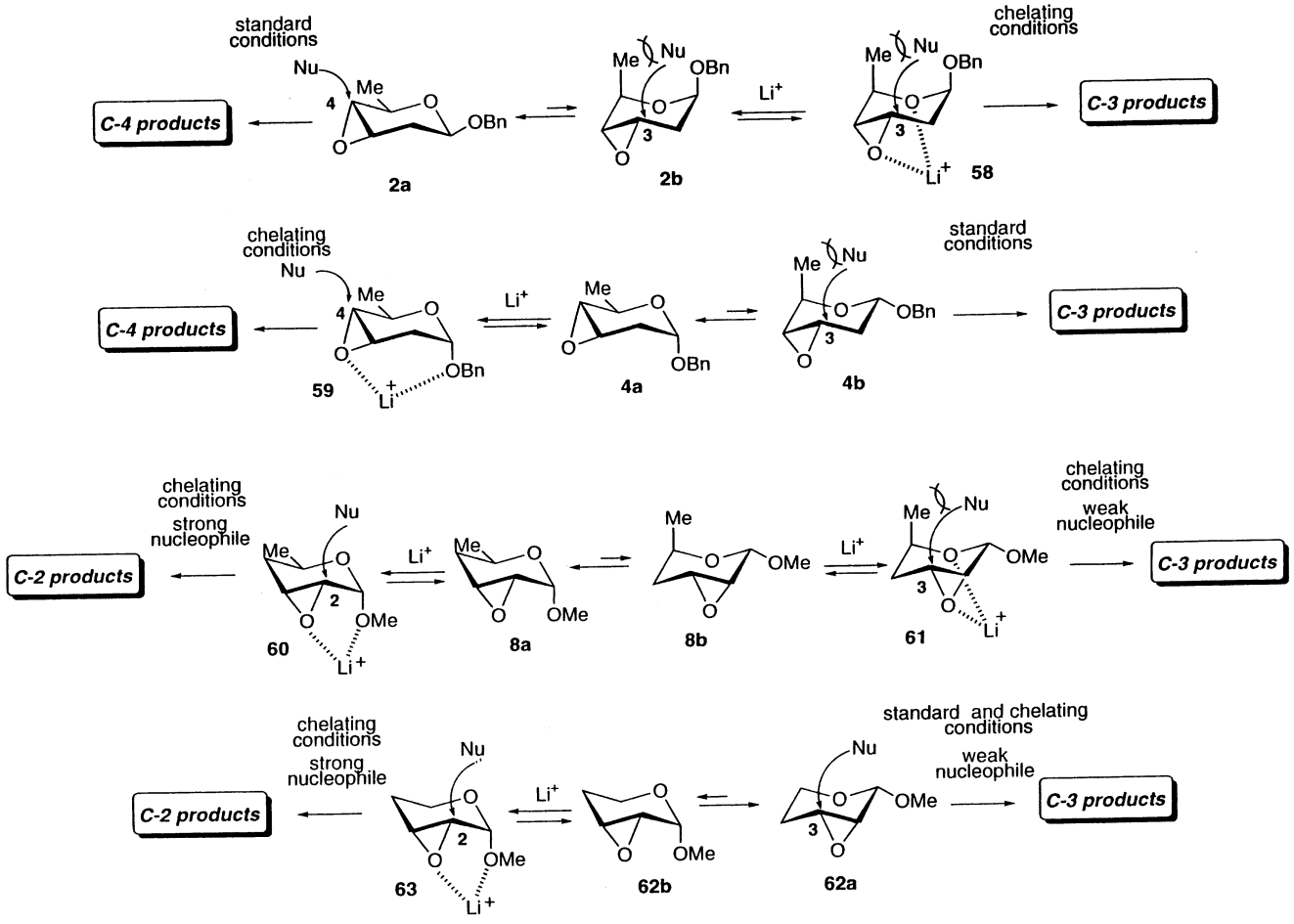
In the presence of a *cis* relationship between the oxirane ring and the methyl group, the regiochemical behavior of the corresponding epoxides **1**, **3**, **5**, and **7** is completely or highly C-3 stereoselective to give *C-3-products*, independently of the operating conditions and position of the acetal OR group with respect to the oxirane ring, *cis* in



Scheme 8.



Scheme 9.



Scheme 10.

epoxides **1** and **5** and *trans* in **3** and **7** (Table 1). With these epoxides, in accordance with the Fürst–Plattner rule, nucleophilic attack occurs on the C(3) oxirane carbon, through the corresponding more stable conformer **a** with the methyl group equatorial,[26] not only under standard conditions, as previously observed with the corresponding methyl glycosides of **1** and **3**,[3] but also under chelating conditions. In fact, under chelating conditions, the incursion of corresponding chelated structures such as **54**–**57**, respectively, in which the more stable conformation **a** is still maintained, is reasonably admitted (Scheme 8).[27,28]

In the presence of a *trans* relationship between the oxirane ring and the methyl group, the regiochemical behavior of the corresponding epoxides **2**, **4**, **6** and **8** is slightly different (Table 2). In these epoxides, nucleophilic attack on the electronically more favored C(3) oxirane carbon, necessarily occurring through the corresponding conformer **b**, suffers from an 1,3-diaxial interaction between the incoming nucleophile and the axial methyl group, as shown in **2**, **4**, **6**, and **8b** (Scheme 9), to the point that, under standard conditions, some amounts (up to 30%) of nucleophilic attack occur at the electronically less favored C(4)- (epoxides **2** and **4**), as previously observed and extensively discussed with the corresponding enantiomeric methyl glycosides,[3] or C(2) oxirane carbon (epoxides **6** and **8**) through the corresponding conformer **a** which allows the methyl group to be equatorial (Scheme 9). As a result of the the absence of a strict correlation between the reactivity of the more stable conformer **a** (methyl group equatorial) and nucleophilic attack on the more reactive C(3)-oxirane carbon, as found in epoxides **1**, **3**, **5**, and **7**, the regioselectivity observed with epoxides **2**, **4**, and **8**, with the only exception of **6**,[29] shows an interesting dependence on the reaction conditions, due to the incursion, under chelating conditions, of chelated bidentate structures able to modify the regiochemical behavior of these epoxides. While in the case of the previously studied epoxide **2**, the incursion of the only possible structure **58** (Scheme 10) determines an increase of *C-3 products*,[2] in the case of epoxide **4**, the incursion of the more stable structure **59** determines a consistent increase of *C-4 products* (Table 2). In this framework, the behavior of epoxide **8** is interesting in which the use of chelating conditions determines an increase of the C-3 selectivity (from 70 to 95%) with weak nucleophiles such as N_3^- and MeOH, while the use of a strong nucleophile such as PhSH determines a partial inversion of regioselectivity and an increase (up to 67%) of the amount of *C-2 products* (Table 2, entries 29–36).

The interesting result obtained with epoxide **8** may be rationalized by admitting, under chelating conditions, the incursion of two different types of chelated structures: structure

60 in which the oxirane oxygen is linked through the metal to the exocyclic OMe group and structure **61** in which the oxirane oxygen and the endocyclic acetal oxygen are coordinated through the metal (Scheme 10). Weak nucleophiles such as N_3^- and MeOH can attack only species **61** still allowing nucleophilic attack on the more reactive C(3)-oxirane carbon (see above) (Table 2, entries 29–32), while strong nucleophiles such as PhSH, as a result of the unfavorable 1,3-diaxial interaction with the axial methyl group occurring in an attack on structure **61**, can take advantage of the presence in the reaction medium of the less hindered structure **60** with consequent preferential attack on the less reactive C(2)-position (Table 2, entries 35 and 36).[30] The regiochemical behavior of epoxide **8** in the reaction with strong and weak nucleophiles is very similar to the one observed in the corresponding opening reactions of the structurally related *cis* epoxide **62**. Also in that case, substantial amounts of *C-2 products* deriving from nucleophilic attack on the electronically less favored C(2)-oxirane carbon were observed only under chelating conditions and with strong nucleophiles such as PhSH, while weak nucleophiles such as MeOH and N_3^- afforded *C-3 products* under any (standard or chelating) conditions. A rationalization based on the incursion of the intermediate chelated bidentate structure **63** and on considerations similar to the ones presently utilized with the structurally related species **60**, admitted from **8**, was correspondingly given (Scheme 10).[1b]

4. Conclusion

A detailed examination of the regiochemical behavior of the branched deoxy anhydro glycosides **1**–**8** allowed the interpretation of the role of the methyl group on the regiochemical behavior of these epoxides. In accordance with previous results from standard opening reactions with the corresponding methyl glycosides of epoxides **1**–**4**,[3] when the methyl is *cis* to the oxirane ring (epoxides **1**, **3**, **5**, and **7**), the nucleophilic attack always occurs in all conditions (standard or chelating) at the C(3)-oxirane carbon, furthest from the electron-withdrawing inductive effect of the acetal functionality, with the epoxide reacting in its more stable conformer **a** (methyl group equatorial). On the contrary, when the methyl group is *trans* to the oxirane ring (epoxides **2**, **4**, **6**, and **8**), it makes the difference: in this case the reactions are *not completely* C-3 regioselective and the oxirane ring opening process *may become* sensitive to reaction conditions. In fact, in these systems, under standard conditions, attack on the electronically more favored C(3)-oxirane carbon necessarily occurs by the less stable conformer **b** with the methyl group axial and consequent unfavorable 1,3-diaxial interaction, to the point that the alternative conformer **a**, bearing the methyl group equatorial, becomes competitive. Attack at the C(2)- (epoxides **6** and **8**) or C(4)-oxirane carbon (epoxides **2** and **4**) is consequently observed to give substantial amounts of *C-2* or *C-4 products*, respectively. Under chelating conditions, the incursion of appropriate intermediate chelated structures can modify the regioselectivity, affording additional amounts of *C-2* (from **8**) or *C-4 products* (from **2** and **4**), respectively.

5. Experimental

5.1. General

Melting points were determined on a Kofler apparatus and are uncorrected. IR spectra for comparison between compounds were registered on a Mattson 3000 FTIR spectrophotometer. ^1H and ^{13}C NMR spectra were determined with a Bruker AC 200 spectrometer on $CDCl_3$ solution using tetramethylsilane as the internal standard. Preparative TLC were performed on 2.0 or 0.5 mm Macherey–Nagel DC-Fertigplatten UV_{254} silica gel plates. All reactions were followed by TLC on Alugram SIL G/UV_{254} silica gel sheets (Machery–Nagel) with detection by UV and/or by a 10% phoshomolybdic acid in EtOH. Silica gel 60 (Machery–Nagel 230–400 mesh) was used for flash chromatography. All the reactions with compounds sensitive to air and/or humidity were carried out under a nitrogen or argon atmosphere and reagents were added via syringe or cannula. Anhydrous solvents were distilled under a nitrogen atmosphere immediately prior to use: THF and toluene from sodium/benzophenone ketyl, and CH_2Cl_2 from CaH_2. Acetylation protocol: the product (0.050 g) in anhydrous pyridine (0.8 mL) was treated at 0°C with Ac_2O (0.5 mL) and the resulting reaction mixture was left 18 h at rt. After dilution with toluene, all solvents were removed under vacuum (rotating evaporator). Glycal (−)-**17**,[7a] dichlorodiol (+)-**30**α[9a] were prepared as previously described.

5.1.1. Diacetate (−)-18. A solution of (−)-tri-(*O*-acetyl)-D-glucal (**12**) (4.0 g, 14.70 mol) in *i*-Pr_2O (25 mL), phosphate buffer (pH 7, 150 mL) and acetone (15 mL) was treated with lipase CCL (1.30 g) and the reaction mixture was stirred at rt for 16 h. Extraction with AcOEt of the filtered (Celite) reaction mixture and evaporation of the washed (saturated aqueous NaCl) organic extracts afforded a crude residue which was subjected to flash chromatography. Elution with an 1:1 hexane/AcOEt mixture afforded pure *(−)-3,4-di-(O-acetyl)-D-glucal* (**18**) (3.10 g, 92% yield), as a liquid (Found: C, 52.38; H, 6.42. $C_{10}H_{14}O_6$ requires C, 52.17; H, 6.13). IR 3465 (OH), 1744 and 1746 cm^{-1} (C=O); $[\alpha]_D^{25}=-55.5$ (*c* 1.38, $CHCl_3$); ^1H NMR δ 6.49 (dd, 1H, *J*=6.1, 1.2 Hz), 5.41–5.50 (m, 1H), 5.22 (dd, 1H, *J*=9.0, 6.5 Hz), 4.81 (dd, 1H, *J*=5.9, 2.8 Hz), 3.98–4.09 (m, 1H), 3.66–3.86 (m, 2H), 2.13 (s, 3H), 2.07 (s, 3H); ^{13}C NMR δ 170.77, 170.60, 145.91, 99.13, 76.72, 68.37, 67.88, 60.63, 21.16, 20.96.

5.1.2. Tosylate (+)-15. A solution of diacetate (−)-**18** (1.70 g, 7.40 mmol) in anhydrous pyridine (15 mL) and anhydrous CH_2Cl_2 (15 mL) was treated at 0°C with TsCl (3.1 g, 16.3 mmol) and the reaction mixture was stirred at the same temperature for 20 h. Dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic solution afforded a crude reaction product which was subjected to flash chromatography. Elution with an 1:1 hexane/AcOEt mixture yielded pure *(+)-3,4-di-(O-acetyl)-6-(O-tosyl)-D-glucal* (**15**)[7b,c] (2.50 g, 88% yield), as a solid, mp 106–108°C (recrystallized from hexane/AcOEt). IR ν 1755 and 1732 cm^{-1} (C=O); $[\alpha]_D^{25}=+14.0$ (*c* 1.2, $CHCl_3$) [lit.[7b] mp 108°C, $[\alpha]_D^{25}=+30$ (*c* 1.1, $CHCl_3$)].

5.1.3. Bromides (+)-19 and (+)-20. Following a previously described procedure,[8] a stirred solution of glycal (−)-**17**[7a] (4.97 g, 23.2 mmol) in MeCN (40 mL) containing benzyl alcohol (3.72 g, 34.5 mmol) was treated at 0°C with NBS (4.95 g, 27.8 mmol) and the resulting reaction mixture was stirred at the same temperature for 1 h. Evaporation of the solvent afforded a residue (7.44 g) consisting of a 73:27 mixture of bromides **20** and **19**, which was subjected to flash chromatography. Elution with a 9:1 hexane/AcOEt afforded pure bromides (+)-**19** (0.57 g, 6% yield) and (+)-**20** (4.80 g, 52% yield).

(+)-Benzyl 3,4-di-(O-acetyl)-2-(β-bromo)-2,6-dideoxy-α-D-mannopyranoside (**20**), a solid, mp 104–106°C (recrystallized from hexane/$CHCl_3$) (Found: C, 51.26; H, 4.96. $C_{17}H_{21}BrO_6$ requires C, 50.89; H, 5.28): $[\alpha]_D^{25}$=+52.3 (*c* 1.8, $CHCl_3$). IR 1745 cm^{-1} (C=O); ^1H NMR δ 7.20–7.40 (m, 5H), 5.13–5.28 (m, 2H), 5.06 (d, 1H, *J*=1.2 Hz), 4.71 (d, 1H, *J*=11.9 Hz), 4.54 (d, 1H, *J*=11.9 Hz), 4.48 (dd, 1H, *J*=3.3, 1.2 Hz), 3.86–4.03 (m, 1H), 2.08 (s, 3H), 2.06 (s, 3H), 1.22 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 170.72, 170.39, 137.13, 129.17, 128.73, 99.57, 71.83, 70.39, 69.93, 67.68, 50.77, 21.48, 21.42, 18.08 (1×Ph signal unresolved).

(+)-Benzyl 3,4-di-(O-acetyl)-2-(α-bromo)-2,6-dideoxy-β-D-glucopyranoside (**19**), a solid, mp 93.5–95°C (recrystallized from hexane/$CHCl_3$) (Found: C, 50.54; H, 5.01. $C_{17}H_{21}BrO_6$ requires C, 50.89; H, 5.28): $[\alpha]_D^{25}$=+22.4 (*c* 0.4, $CHCl_3$). IR 1749 cm^{-1} (C=O); ^1H NMR δ 7.30–7.45 (m, 5H), 5.24 (dd, 1H, *J*=10.7, 9.5 Hz), 4.92 (d, 1H, *J*=11.8 Hz), 4.68 (d, 1H, *J*=11.8 Hz), 4.74 (t, 1H, *J*=9.5 Hz), 4.60 (d, 1H, *J*=8.7 Hz), 3.84 (dd, 1H, *J*=10.7, 8.7 Hz), 3.59 (dq, 1H, *J*=9.5, 6.2 Hz), 2.08 (s, 3H), 2.03 (s, 3H), 1.27 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 170.51, 170.38, 137.01, 129.07, 128.75, 101.28, 75.33, 74.87, 71.93, 70.68, 50.53, 21.30, 17.93 (1×Ph and 1×Me signals unresolved).

5.1.4. Diacetate (+)-21. A solution of bromide (+)-**20** (5.97 g, 14.9 mmol) in anhydrous benzene (80 mL) was treated with Bu_3SnH (6.50 g, 22.3 mmol) in the presence of a catalytic amount of benzoyl peroxide and the resulting reaction mixture was refluxed for 1 h. After cooling, evaporation of the solvent afforded a residue which was dissolved in MeCN. Evaporation of the washed (petroleum ether) acetonitrile solution yielded a crude liquid product consisting of the diacetate (+)-**21** (4.75 g, 99% yield) practically pure which was directly utilized in the next step without any further purification. An analytical sample of crude (+)-**21** (0.10 g) was purified by preparative TLC with an 85:15 hexane/AcOEt mixture as the eluant. Extraction of the most intense band afforded pure *(+)-benzyl 3,4-di-(O-acetyl)-2,6-dideoxy-α-D-glucopyranoside* (**21**), as a liquid (0.076 g, 76% yield) (Found: C, 63.07; H, 6.51. $C_{17}H_{22}O_6$ requires C, 63.34; H, 6.88): $[\alpha]_D^{25}$=+142.1 (*c* 0.9, $CHCl_3$). IR 1745 cm^{-1} (C=O); ^1H NMR δ 7.20–7.41 (m, 5H), 5.32 (ddd, 1H, *J*=11.6, 9.8, 5.4 Hz), 4.96 (unresolved dd, 1H, *J*=3.0 Hz), 4.76 (t, 1H, *J*=9.8 Hz), 4.68 (d, 1H, *J*=12.1 Hz), 4.48 (d, 1H, *J*=12.1 Hz), 3.90 (dq, 1H, *J*=9.8, 6.1 Hz), 2.27 (ddd, 1H, *J*=12.9, 5.4, 1.2 Hz), 2.05 (s, 3H), 2.00 (s, 3H), 1.81 (ddd, 1H, *J*=12.9, 11.6, 3.7 Hz), 1.17 (d, 3H, *J*=6.1 Hz); ^{13}C NMR δ 170.86, 138.03, 129.04, 128.44, 128.38, 96.54, 75.45, 69.70, 69.57, 66.41, 35.89, 21.65, 21.48, 18.16 (1×CO signal unresolved).

5.1.5. Diol (+)-22α. The treatment of a solution of diacetate (+)-**21** (0.56 g, 1.74 mmol) in MeOH (20 mL) with MeONa (0.010 g) under stirring for 18 h at rt afforded, after evaporation of the filtered organic solution, a crude product consisting of diol (+)-**22**α (0.40 g), which was filtered through a short silical gel column. Elution with AcOEt afforded pure *(+)-benzyl 2,6-dideoxy-α-D-glucopyranoside* (**22**α) (0.34 g, 82% yield), as a solid, mp 112–114.5°C (recrystallized from hexane/AcOEt) (Found: C, 65.44; H, 6.34. $C_{13}H_{18}O_4$ requires C, 65.53; H, 7.61): $[\alpha]_D^{25}$=+123.4 (*c* 1.1, $CHCl_3$). IR 3365 cm^{-1} (OH); ^1H NMR δ 7.20–7.41 (m, 5H), 4.93 (unresolved dd, 1H, *J*=3.1 Hz), 4.67 (d, 1H, *J*=11.9 Hz), 4.44 (d, 1H, *J*=11.9 Hz), 3.85–4.05 (m, 1H), 3.70 (dq, 1H, *J*=9.0, 6.2 Hz), 3.11 (t, 1H, *J*=9.0 Hz), 2.17 (ddd, 1H, *J*=12.8, 5.4, 1.2 Hz), 1.70 (ddd, 1H, *J*=12.8, 11.6, 3.6 Hz), 1.30 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 138.22, 129.04, 128.49, 128.35, 97.08, 78.38, 69.59, 69.41, 68.46, 38.29, 18.41.

5.1.6. Monoprotection of diol (+)-22α. A solution of diol (+)-**22**α (0.50 g, 2.10 mmol) in anhydrous DMF (11 mL) containing imidazole (0.29 g, 4.20 mmol) was treated at 0°C with TBDMS-Cl (0.32 g, 2.10 mmol) and the resulting reaction mixture was stirred at rt for 18 h. Dilution with ether and evaporation of the washed (water) organic solvent afforded a crude product (0.73 g, 99% yield) mostly consisting of alcohol (+)-**23**, which was directly utilized in the next step without any further purification. An analytical sample of crude (+)-**23** was subjected to flash chromatography. Elution with a 9.5:0.5 hexane/AcOEt mixture afforded pure *(+)-benzyl 3-(O-t-butyldimethylsilyl)-2,6-dideoxy-α-D-glucopyranoside* (**23**), as a liquid (Found: C, 64.91; H, 9.28. $C_{19}H_{32}O_4Si$ requires C, 64.73; H, 9.15): $[\alpha]_D^{25}$=+80.15 (*c* 1.8, $CHCl_3$). IR 3499 cm^{-1} (OH); ^1H NMR δ 7.20–7.40 (m, 5H), 4.90 (unresolved dd, 1H, *J*=2.8 Hz), 4.68 (d, 1H, *J*=12.2 Hz), 4.45 (d, 1H, *J*=12.2 Hz), 3.96 (ddd, 1H, *J*=11.3, 9.0, 5.1 Hz), 3.73 (dq, 1H, *J*=9.0, 6.2 Hz), 3.13 (td, 1H, *J*=9.0, 2.0 Hz), 2.06 (ddd, 1H, *J*=12.6, 5.1, 1.2 Hz), 1.70 (ddd, 1H, *J*=12.6, 11.3, 3.7 Hz), 1.29 (d, 3H, *J*=6.2 Hz), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR δ 138.60, 129.02, 128.34, 128.23, 97.28, 78.63, 71.20, 69.26, 68.22, 39.26, 26.44, 18.56, 18.66, −3.51, −3.96.

5.1.7. Mesylate (+)-24. A solution of alcohol (+)-**23** (0.49 g, 1.40 mmol) in anhydrous pyridine (6 mL) was treated at 0°C with MsCl (0.64 g, 5.6 mmol) and the resulting reaction mixture was stirred at rt for 18 h. Dilution with ether and evaporation of the washed (water) organic solvent afforded a crude product (0.60 g) mostly consisting of mesylate (+)-**24** which was filtered through a short silica gel column. Elution with an 85:15 hexane/AcOEt mixture afforded pure *(+)-benzyl 3-(O-t-butyldimethylsilyl)-4-(O-mesyl)-2,6-dideoxy-α-D-glucopyranoside* (**24**) (0.56 g, 90% yield), as a liquid (Found: C, 55.66; H, 7.92. $C_{20}H_{34}O_6SSi$ requires C, 55.78; H, 7.96): $[\alpha]_D^{25}$=+65.3 (*c* 1.4, $CHCl_3$); ^1H NMR δ 7.20–7.40 (m, 5H), 4.90 (unresolved dd, 1H, *J*=2.6 Hz), 4.65 (d, 1H, *J*=12.2 Hz), 4.46 (d, 1H, *J*=12.2 Hz), 4.10–4.30 (m, 2H), 3.87 (dq, 1H, *J*=9.2, 6.3 Hz), 3.07 (s, 3H), 2.19 (ddd, 1H, *J*=13.1, 4.6, 1.1 Hz), 1.75 (ddd, 1H, *J*=13.1, 10.9, 3.6 Hz), 1.34 (d, 3H, *J*=6.3 Hz), 0.90 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR δ 138.24, 129.10, 128.40, 128.32, 96.67, 87.10, 69.58,

68.50, 66.96, 40.32, 39.70, 26.57, 18.70, −3.16, −3.77 (1×Me signals unresolved).

5.1.8. Hydroxy mesylate (+)-25. A solution of mesylate (+)-**24** (0.47 g, 1.06 mmol) in anhydrous THF (15 mL) was treated at 0°C with 1 M TBAF in THF (2.2 mL, 2.20 mmol) and the resulting reaction mixture was stirred at the same temperature for 20 min. Dilution with ether and evaporation of the washed (water) organic solvent afforded a crude product (0.40 g) mostly consisting of hydroxy mesylate (+)-**25** which was subjected to flash chromatography. Elution with a 70:30 hexane/AcOEt mixture afforded pure *(+)-benzyl 4-(O-mesyl)-2,6-dideoxy-α-D-glucopyranoside* (**25**) (0.24 g, 72% yield), as a solid, mp 64.5–66°C (recrystallized from hexane/AcOEt) (Found: C, 53.39; H, 6.02. $C_{14}H_{20}O_6S$ requires C, 53.15; H, 6.37): $[\alpha]_D^{25}$=+110.2 (*c* 1.0, $CHCl_3$). IR 3450 cm^{-1} (OH); ^1H NMR δ 7.20–7.40 (m, 5H), 4.95 (unresolved dd, 1H, *J*=2.9 Hz), 4.65 (d, 1H, *J*=11.9 Hz), 4.45 (d, 1H, *J*=11.9 Hz), 4.10–4.30 (m, 2H), 3.94 (dq, 1H, *J*=9.1, 6.2 Hz), 3.15 (s, 3H), 2.28 (ddd, 1H, *J*=13.1, 5.0, 1.2 Hz), 1.75 (ddd, 1H, *J*=13.1, 11.1, 3.6 Hz), 1.32 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 137.97, 129.16, 128.51, 96.75, 86.80, 69.83, 67.57, 66.01, 39.28, 38.89, 18.34 (1×Ph signal unresolved).

5.1.9. Epoxide (+)-3. A solution of hydroxy mesylate (+)-**25** (0.24 g, 0.76 mmol) in anhydrous toluene (10 mL) was treated with Amberlyst IRA-400 (OH^-) (0.24 g) and the resulting suspension was stirred at rt for 1 h. Evaporation of the filtered organic solution afforded pure *(+)-benzyl 3,4-anhydro-2,6-dideoxy-α-D-galactopyranoside* (**3**) (0.164 g, 98% yield), as a solid, mp 31–34°C (recrystallized from hexane) (Found: C, 70.55; H, 7.28. $C_{13}H_{16}O_3$ requires C, 70.89; H, 7.32): $[\alpha]_D^{25}$=+110.8 (*c* 0.5, $CHCl_3$); ^1H NMR δ 7.20–7.40 (m, 5H), 4.81 (d, 1H, *J*=5.0 Hz), 4.69 (d, 1H, *J*=11.9 Hz), 4.47 (d, 1H, *J*=11.9 Hz), 4.15 (q, 1H, *J*=6.7 Hz), 3.34 (t, 1H, *J*=4.4 Hz), 3.05 (d, 1H, *J*=4.4 Hz), 2.16 (dd, 1H, *J*=15.7, 5.0 Hz), 1.98 (ddd, 1H, *J*=15.7, 5.0, 1.0 Hz), 1.36 (d, 3H, *J*=6.7 Hz); ^{13}C NMR δ 138.17, 129.11, 128.52, 128.47, 94.16, 69.69, 61.94, 53.47, 49.39, 29.04, 18.27.

5.1.10. Monotosylation of diol (+)-22α. A solution of diol (+)-**22**α (1.19 g, 5.0 mmol) in anhydrous pyridine (25 mL) was treated at 0°C with TsCl (1.01 g, 5.30 mmol) and the resulting reaction mixture was stirred at rt for 5 days. Dilution with ether and evaporation of the washed (water) organic solvent afforded a crude residue (1.87 g) consisting of a 73:17:10 mixture of monotosylates (+)-**26** and (+)-**27** (81% yield) and ditosylate (+)-**28** which was directly used in the next step without any further purification. An analytical sample (0.35 g) of this mixture was subjected to preparative TLC using an 1:1 petroleum ether/Et_2O mixture as the eluant. Extration of the three most intense bands (the fastest and slowest moving bands contained **28** and **27**, respectively) afforded pure monotosylates (+)-**26** (0.182 g) and (+)-**27** (0.041 g), and ditosylate (+)-**28** (0.020 g).

(+)-Benzyl 3-(O-tosyl)-2,6-dideoxy-α-D-glucopyranoside (**26**), a liquid (Found: C, 61.56; H, 6.05. $C_{20}H_{24}O_6S$ requires C, 61.21; H, 6.16): $[\alpha]_D^{25}$=+107.7 (*c* 1.0, $CHCl_3$). IR 3524 cm^{-1} (OH); ^1H NMR δ 7.82 (d, 2H, *J*=8.3 Hz), 7.20–7.42 (m, 7H), 4.86 (dd, 1H, *J*=3.4, 1.2 Hz), 4.80 (ddd, 1H, *J*=11.6, 9.0, 5.4 Hz), 4.63 (d, 1H, *J*=12.1 Hz), 4.41 (d, 1H, *J*=12.1 Hz), 3.72 (dq, 1H, *J*=9.1, 6.2 Hz), 3.32 (t, 1H, *J*=9.1 Hz), 2.45 (s, 3H), 2.11 (ddd, 1H, *J*=12.8, 5.4, 1.2 Hz), 1.83 (ddd, 1H, *J*=12.8, 11.6, 3.6 Hz), 1.29 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 145.77, 138.00, 134.03, 130.59, 129.05, 128.57, 128.39, 96.42, 81.39, 75.27, 69.41, 68.47, 36.61, 22.37, 18.46 (1×Ph signal unresolved).

(+)-Benzyl 4-(O-tosyl)-2,6-dideoxy-α-D-glucopyranoside (**27**), a liquid (Found: C, 61.34; H, 6.21. $C_{20}H_{24}O_6S$ requires C, 61.21; H, 6.16): $[\alpha]_D^{25}$=+83.2 (*c* 2.4, $CHCl_3$). IR 3489 cm^{-1} (OH); ^1H NMR δ 7.84 (d, 2H, *J*=8.4 Hz), 7.20–7.45 (m, 7H), 4.93 (unresolved dd, 1H, *J*=3.2 Hz), 4.61 (d, 1H, *J*=11.9 Hz), 4.42 (d, 1H, *J*=11.9 Hz), 4.08–4.26 (m, 2H), 3.79 (dq, 1H, *J*=9.4, 6.1 Hz), 2.45 (s, 3H), 2.26 (ddd, 1H, *J*=13.3, 4.8, 1.1 Hz), 1.74 (ddd, 1H, *J*=13.3, 11.3, 3.7 Hz), 1.12 (d, 3H, *J*=6.1 Hz); ^{13}C NMR δ 146.06, 138.02, 133.75, 130.59, 129.10, 128.68, 128.47, 128.41, 96.79, 87.54, 69.76, 67.39, 65.69, 38.11, 22.37, 18.22.

(+)-Benzyl 3,4-di-(O-tosyl)-2,6-dideoxy-α-D-glucopyranoside (**28**), a liquid (Found: C, 59.03; H, 5.27. $C_{27}H_{30}O_8S_2$ requires C, 59.32; H, 5.53): $[\alpha]_D^{25}$=+86.0 (*c* 1.9, $CHCl_3$); ^1H NMR δ 7.80 (d, 2H, *J*=8.4 Hz), 7.62 (d, 2H, *J*=8.4 Hz), 7.20–7.42 (m, 9H), 4.71–4.90 (m, 2H), 4.57 (d, 1H, *J*=12.0 Hz), 4.40 (d, 1H, *J*=12.0 Hz), 4.43 (t, 1H, *J*=9.4 Hz), 3.82 (dq, 1H, *J*=9.4, 6.3 Hz), 2.45 (s, 3H), 2.43 (s, 3H), 2.22 (ddd, 1H, *J*=13.1, 5.3, 1.3 Hz), 1.83 (ddd, 1H, *J*=13.1, 11.8, 3.4 Hz), 1.22 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 145.64, 145.59, 137.75, 134.55, 134.03, 130.42, 129.10, 128.78, 128.54, 128.35, 96.06, 81.86, 76.48, 69.69, 67.00, 37.17, 22.40, 18.54 (2×Ph and 1×Me signals unresolved).

5.1.11. Epoxide (+)-4. A solution of the 73:17:10 mixture of monotosylates (+)-**26** and (+)-**27** and ditosylate (+)-**28** (1.42 g), in anhydrous benzene (40 mL) was treated at rt with Amberlyst IRA-400 (OH^-) (1.40 g) and the reaction suspension was stirred at the same temperature for 1 h. Evaporation of the filtered organic solution afforded a crude product (0.80 g) consisting of a 73:17:10 mixture of epoxides (+)-**4** and (+)-**3** and ditosylate (+)-**28** which was subjected to flash chromatography. Elution with an 85:15 hexane/AcOEt mixture afforded pure epoxide (+)-**3** (0.11 g, 15% yield), ditosylate (+)-**28** (0.071 g) and *(+)-benzyl 3,4-anhydro-2,6-dideoxy-α-D-allopyranoside* (**4**), as a liquid (0.40 g, 55% yield) (Found: C, 70.65; H, 7.06. $C_{13}H_{16}O_3$ requires C, 70.89; H, 7.32): $[\alpha]_D^{25}$=+136.3 (*c* 1.6, $CHCl_3$); ^1H NMR δ 7.20–7.42 (m, 5H), 4.78 (dd, 1H, *J*=4.7, 3.0 Hz), 4.72 (d, 1H, *J*=12.3 Hz), 4.46 (d, 1H, *J*=12.3 Hz), 4.21 (q, 1H, *J*=7.0 Hz), 3.21–3.30 (m, 1H), 3.00 (dd, 1H, *J*=4.4 Hz), 2.00–2.24 (m, 2H), 1.38 (d, 3H, *J*=7.0 Hz); ^{13}C NMR δ 138.28, 128.96, 128.55, 128.22, 93.51, 69.86, 65.29, 54.29, 48.95, 29.83, 19.34.

5.1.12. Hydrogenolysis of dichloro diol (+)-30α. Following a previously described procedure,[9a] a solution of dichloro diol (+)-**30**α (2.0 g, 8.66 mmol) in anhydrous EtOH (20 mL) containing KOH (1.80 g, 32.14 mmol) was stirred at rt under an hydrogen atmosphere in the presence of Ni-Raney (9.20 g) for 24 h. Evaporation of the filtered (Celite) and neutralized (aqueous 10% HCl) organic

solution afforded a crude product which was taken up in boiling $CHCl_3$. Evaporation of the filtered organic solution afforded a crude product (1.40 g) consisting of a 9:1 mixture of diol (+)-**31**α and oxabicyclic compound (+)-**33** which was subjected to flash chromatography. Elution with a 7:3 CH_2Cl_2/acetone mixture afforded pure diol (+)-**31**α (1.12 g, 80% yield) and the oxabicyclic compound (+)-**33** (0.13 g, 9% yield).

(+)-Methyl 4,6-dideoxy-α-D-glucopyranoside (**31**α),[9] a solid, mp 106–107°C, $[\alpha]_D^{25}$=+178.3 (*c* 1.6, MeOH) [lit.[9b,c] mp 107–109°C, $[\alpha]_D^{23}$=+171 (*c* 1.0, MeOH);[9a] mp 106–107°C, $[\alpha]_D^{24}$=+178.5 (*c* 0.9, MeOH)[9b]].

(+)-Methyl 4-deoxy-3,6-anhydro-α-D-glucopyranoside (**33**), a solid, mp 95–96°C (recrystallized from hexane/Et_2O) (Found: C, 52.41; H, 7.86. $C_7H_{12}O_4$ requires C, 52.49; H, 7.55): $[\alpha]_D^{25}$=+109.0 (*c* 3.6, $CHCl_3$). IR 3460 cm^{-1} (OH); ^1H NMR δ 4.73 (d, 1H, *J*=2.8 Hz), 4.47–4.57 (m, 2H), 4.09 (dd, 1H, *J*=10.0, 1.2 Hz), 3.79 (dd, 1H, *J*=10.0, 2.8 Hz), 3.60–3.80 (m, 1H), 3.55 (s, 3H), 2.53 (dt, 1H, *J*=12.2, 1.3 Hz), 1.61 (ddd, 1H, *J*=12.2, 5.9, 2.6 Hz); ^{13}C NMR δ 98.14, 77.09, 74.66, 72.00, 69.02, 57.46, 31.70.

5.1.13. Reaction of the dichloro diol (+)-30α with Bu_3SnH. Following a previously described procedure,[9c] a solution of dichloro diol (+)-**30**α (0.70 g, 3.03 mmol) in anhydrous toluene (14 mL) was treated with Bu_3SnH (3.62 g, 12.4 mmol) in the presence of a catalytic amount of AIBN and the resulting reaction mixture was refluxed for 18 h. After cooling, evaporation of the solvent afforded an oily residue which solidified on treatment with petroleum ether. Filtration gave a solid consisting of an almost 1:1 mixture of diol (+)-**31**α and monochloro derivative **32**:[9e] ^1H NMR δ 4.83 (d, 1H, *J*=3.8 Hz), 3.56 (d, 2H, *J*=5.4 Hz), 3.44 (s, 3H), 2.10 (ddd, 1H, *J*=12.6, 5.0, 2.1 Hz), 1.50 (unresolved dt, 1H, *J*=12.3, 11.7 Hz).

5.1.14. Monoacetate (+)-34α. A solution of diol (+)-**31**α (0.10 g, 0.62 mmol) in a 7:3 mixture of vinyl acetate and THF (16 mL) was treated at 37°C with lipase PS immobilized on Hyflo Super Cell (0.62 g). After 24 h stirring at the same temperature, evaporation of the solvent afforded a crude reaction product consisting of monoacetate (+)-**34**α (0.12 g) which was subjected to flash chromatography. Elution with an 8:2 CH_2Cl_2/acetone mixture afforded pure *(+)-methyl 2-(O-acetyl)-4,6-dideoxy-α-D-glucopyranoside* (**34**α), as a liquid (0.088 g, 70% yield) (Found: C, 52.60; H, 7.71. $C_9H_{16}O_5$ requires C, 52.93; H, 7.90): α=+154.0 (*c* 1.6, $CHCl_3$). IR 3471 (OH) and 1740 cm^{-1} (CO); ^1H NMR δ 4.80 (d, 1H, *J*=3.6 Hz), 4.55 (dd, 1H, *J*=9.8, 3.6 Hz), 4.02 (ddd, 1H, *J*=11.6, 9.8, 5.4 Hz), 3.86 (dqd, 1H, *J*=11.6, 6.3, 2.5 Hz), 3.29 (s, 3H), 2.08 (s, 3H), 1.99 (ddd, 1H, *J*=12.7, 5.4, 2.5 Hz), 1.38 (dt, 1H, *J*=12.7, 11.6 Hz), 1.15 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 171.93, 98.17, 76.86, 66.41, 64.21, 55.64, 41.57, 21.70, 21.36.

5.1.15. Mesylate (+)-35α. A solution of acetate (+)-**34**α (0.086 g, 0.42 mmol) in anhydrous pyridine (3.0 mL) was treated at 0°C, under stirring, with MsCl (0.096 g, 0.84 mmol). After 18 h at the same temperature, dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic solution afforded a crude product consisting of mesylate (+)-**35**α (0.114 g) which was subjected to flash chromatography. Elution with an 1:1 hexane/AcOEt mixture afforded pure *(+)-methyl 2-(O-acetyl)-3-(O-mesyl)-4,6-dideoxy-α-D-glucopyranoside* (**35**α) (0.092 g, 77% yield), as a solid, mp 56–59°C (recrystallized from hexane/CH_2Cl_2) (Found: C, 42.84; H, 6.66. $C_{10}H_{18}O_7S$ requires C, 42.55; H, 6.43): $[\alpha]_D^{25}$=+138.0 (*c* 1.0, $CHCl_3$). IR 1748 cm^{-1}(CO); ^1H NMR δ 4.95 (ddd, 1H, *J*=11.4, 10.0, 5.2 Hz), 4.86 (d, 1H, *J*=3.5 Hz), 4.76 (dd, 1H, *J*=10.0, 3.5 Hz), 3.90 (dqd, 1H, *J*=11.4, 6.3, 2.2 Hz), 3.30 (s, 3H), 2.96 (s, 3H), 2.24 (ddd, 1H, *J*=12.7, 5.2, 2.3 Hz), 2.06 (s, 3H), 1.65 (dt, 1H, *J*=12.7, 11.4 Hz), 1.17 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 170.67, 98.11, 76.39, 72.64, 63.55, 55.77, 40.38, 38.96, 21.55, 21.11.

5.1.16. Epoxide (+)-8. A solution of mesylate (+)-**35**α (0.23 g, 0.81 mmol) in MeOH (5 mL) was treated at rt under stirring with MeONa (0.020 g). After 2 h stirring, evaporation of the neutralized (10% aqueous HCl) organic solvent afforded a crude reaction product (0.19 g) consisting of hydroxy mesylate **36**α [IR 3468 cm^{-1} (OH)][11b] which was dissolved in anhydrous benzene (7 mL) and treated under stirring with *t*-BuOK (0.18 g, 1.60 mmol). After 30 min stirring ar rt, evaporation of the filtered organic solution afforded pure *(+)-methyl 2,3-anhydro-4,6-dideoxy-α-D-allopyranoside* (**8**)[9b,11] (0.076 g, 65% yield), as a liquid, $[\alpha]_D^{25}$=+72 (*c* 1.0, $CHCl_3$) [lit.[9b,11a,b] $[\alpha]_D^{24}$=+75 (*c* 1.0, $CHCl_3$);[9b] $[\alpha]_D^{18}$=+66.8 (*c* 1.2, $CHCl_3$);[11a] $[\alpha]_D^{23}$=+77 (*c* 1.3, $CHCl_3$)[11b]].

5.1.17. Reaction of diol (+)-31α with PPh_3-DEAD. A solution of diol (+)-**31**α (1.46 g, 9.0 mmol) in anhydrous benzene (45 mL) containing 4 Å molecular sieves was treated under stirring with PPh_3 (2.59 g, 9.90 mmol) and DEAD (1.72 g, 9.90 mmol). After precipitation of white needles had occured, the reaction mixture was refluxed for 24 h, then cooled and evaporated to afford a crude residue which was taken up with Et_2O. Evaporation of the filtered organic solution afforded a liquid product which was distilled (Kügel–Rohr) to give pure epoxide (+)-**8** (0.80 g, 62% yield), as a liquid, bp 130°C (13 mmHg).[9b,11]

5.1.18. Epoxide (+)-7. A solution of diol (+)-**31**α (1.06 g, 6.54 mmol) in anhydrous pyridine (20 mL) was treated at rt under stirring with TsCl (1.49 g, 7.83 mmol). After 4 days stirring at the same temperature, dilution with CH_2Cl_2 and evaporation of the washed (water) organic solution afforded a crude oily residue consisting of an 85:15 mixture of monotosylates **37** and **38** (1.96 g, 95% yield) which was dissolved in anhydrous benzene (40 mL) and treated at rt with *t*-BuOK (1.10 g, 9.81 mmol). After 2 h stirring at the same temperature, evaporation of the filtered organic solution afforded a crude product (0.72 g) consisting of an 80:20 mixture of epoxides (+)-**7** and (+)-**8**, which was subjected to flash chromatography. Elution with an 8:2 hexane/AcOEt mixture afforded pure epoxide (+)-**8** (0.090 g, 9% yield) and *(+)-methyl 2,3-anhydro-4,6-dideoxy-α-D-mannopyranoside* (**7**)[9b,11b] (0.55 g, 58% yield), as a liquid, $[\alpha]_D^{25}$=+52 (*c* 1.0, $CHCl_3$) [lit.[9b,11b] $[\alpha]_D^{25}$=+55 (*c* 2.7, $CHCl_3$);[9b] $[\alpha]_D^{23}$=+52 (*c* 1.4, $CHCl_3$)[11b]].

5.1.19. Diacetate (+)-39α. A solution of diol (+)-**31**α (1.0 g, 6.17 mmol) in anhydrous pyridine (20 mL) was treated with Ac_2O (4 mL) and the reaction mixture was stirred at rt for 24 h. Evaporation of the organic solvent afforded the diacetate (+)-**39**α (1.35 g, 89% yield), practically pure as a liquid, which was directly used in the next step without any further purification. An analytical sample was subjected to preparative TLC with an 8:2 CH_2Cl_2/MeCN mixture. Extraction of the most intense band afforded pure *(+)-methyl 2,3-di-(O-acetyl)-4,6-dideoxy-α-D-glucopyranoside* (**39**α),[16a] as a liquid, $[\alpha]_D^{25}$=+163.5 (*c* 2.4, MeOH).

5.1.20. Reaction of diacetate (+)-39α with lipase PPL. A solution of diacetate (+)-**39**α (0.093 g, 0.38 mmol) in acetone (3 mL) and phosphate buffer (pH 7, 30 mL) was treated with crude lipase PPL type II immobilized on Hyflo Super Cell (0.50 g) and the reaction mixture was incubated, under stirring, at 37°C. When TLC analysis showed that all the starting material was consumed, evaporation of the filtered organic solvent afforded a crude oily product (0.077 g) consisting of a 60:40 mixture of hydroxy acetates **40**α and **34**α which was subjected to flash chromatography. Elution with an 1:1 hexane/AcOEt mixture afforded pure hydroxy acetates (+)-**34**α (0.024 g, 31% yield) and *methyl 3-(O-acetyl)-4,6-dideoxy-α-D-glucopyranoside* (**40**α) (0.036 g, 46% yield), as a liquid (Found: C, 52.72; H, 7.98. $C_9H_{16}O_5$ requires C, 52.93; H, 7.90). IR 3466 (OH) and 1738 cm^{-1} (CO); ^1H NMR δ 4.99 (ddd, 1H, *J*=11.6, 9.8, 5.0 Hz), 4.71 (d, 1H, *J*=3.8 Hz), 3.88 (dqd, 1H, *J*=11.6, 6.3, 2.0 Hz), 3.44–3.56 (m, 1H), 3.35 (s, 3H), 2.03 (s, 3H), 1.97 (ddd, 1H, *J*=12.7, 5.0, 2.0 Hz), 1.32 (dt, 1H, *J*=12.7, 11.6 Hz), 1.14 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 171.84, 100.72, 72.30, 72.07, 64.29, 55.89, 38.54, 21.91, 21.35.

5.1.21. Diacetate (+)-39β. A solution of diacetate (+)-**39**α (2.46 g, 10.0 mmol) in anhydrous toluene (95 mL) was treated at rt under stirring with $(CH_3)_3SiI$ (5.7 mL, 40.0 mmol) and the reaction mixture was stirred at the same temperature for 24 h. Dilution with $CHCl_3$ and evaporation of the washed (water, 10% aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$) organic solution, afforded a crude residue which was immediately dissolved in MeOH (200 mL), treated with Ag_2CO_3 (3.58 g, 12.98 mmol) and the reaction mixture was gently refluxed for 4 h. After cooling, evaporation of the filtered (Celite) organic solvent afforded a crude liquid product consisting of the diacetate (+)-**39**β[16b] (2.40 g, 97% yield) which was directly utilized in the next step. An analytical sample was subjected to preparative TLC with an 8:2 CH_2Cl_2/MeCN mixture as the eluant. Extraction of the most intense band afforded pure *(+)-methyl 2,3-di-(O-acetyl)-4,6-dideoxy-β-D-glucopyranoside* (**39**β), as a liquid, $[\alpha]_D^{25}$=+10.5 (*c* 0.4, dioxane) [lit.[16b] $[\alpha]_D^{25}$=+11.3 (*c* 0.3, dioxane)].

5.1.22. Diol (−)-31β. A solution of diacetate (+)-**39**β (2.46 g, 10.0 mmol) in MeOH (50 mL) was treated with MeONa (0.15 g). After 1 h stirring at rt, the solution was neutralized (10% aqueous HCl) and evaporated to give *(−)-methyl 4,6-dideoxy-β-D-glucopyranoside* (**31**β)[19] (1.35 g, 83% yield), as a solid, mp 100–102°C, $[\alpha]_D^{25}$=−59.7 (*c* 1.2, $CHCl_3$) (lit.[19] mp 104–105°C, $[\alpha]_D^{20}$=−60.4 (*c* 1.2, $CHCl_3$).

5.1.23. Monoacetate (+)-40β. Proceeding as previously described for the corresponding reaction of diol (+)-**31**α the treatment of a solution of diol (−)-**31**β (0.663 g, 4.09 mmol) in a 7:3 mixture of vinyl acetate and THF (100 mL) with lipase PS immobilized on Hyflo Super Cell (4.0 g) at 37°C under stirring for 24 h afforded a crude reaction product consisting of monoacetate (+)-**40**β (0.83 g, 99% yield) which was directly utilized in the next step. An analytical sample (0.080 g) was subjected to preparative TLC with an 8:2 CH_2Cl_2/CH_3CN mixture as the eluant. Extraction of the most intense band afforded pure *(+)-methyl 3-(O-acetyl)-4,6-dideoxy-β-D-glucopyranoside* (**40**β) (0.064 g), as a liquid (Found: C, 52.77; H, 7.66. $C_9H_{16}O_5$ requires C, 52.93; H, 7.90): $[\alpha]_D^{25}$=+8.2 (*c* 1.2, $CHCl_3$). IR 3460 (OH) and 1736 cm^{-1} (CO); ^1H NMR δ 4.86 (ddd, 1H, *J*=11.4, 9.3, 5.2 Hz), 4.18 (d, 1H, *J*=7.8 Hz), 3.65 (dqd, 1H, *J*=11.4, 6.2, 1.9 Hz), 3.43 (dd, 1H, *J*=9.3, 7.8 Hz), 3.56 (s, 3H), 2.10 (s, 3H), 2.04–2.18 (m, 1H), 1.41 (dt, 1H, *J*=12.7, 11.4 Hz), 1.27 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 171.58, 104.52, 73.66, 73.53, 68.38, 57.60, 38.35, 21.71, 21.27.

5.1.24. Mesylate (−)-43β. A solution of acetate (+)-**40**β (0.83 g, 4.07 mmol) in anhydrous pyridine (20 mL) was treated at 0°C under stirring with MsCl (1.83 g, 16.0 mmol) and the reaction mixture was stirred at rt for 3 h. Dilution with ice-water and CH_2Cl_2 and evaporation of the washed (water) organic solvent afforded a crude solid residue (1.10 g) which was recrystallized from hexane/AcOEt to give pure *(−)-methyl 3-(O-acetyl)-2-(O-mesyl)-4,6-dideoxy-β-D-glucopyranoside* (**43**β) (0.79 g, 69% yield), as a solid mp 76–79.5°C (Found: C, 42.79; H, 6.24. $C_{10}H_{18}O_7S$ requires C, 42.55; H, 6.43): $[\alpha]_D^{25}$=−18.1 (*c* 1.0, $CHCl_3$). IR 1741 cm^{-1} (CO); ^1H NMR δ 4.30–4.45 (m, 2H), 4.93–5.12 (m, 1H), 3.67 (dqd, 1H, *J*=11.6, 6.2, 1.9 Hz), 3.55 (s, 3H), 3.07 (s, 3H), 2.16 (ddd, 1H, *J*=13.0, 5.4, 1.9 Hz), 2.11 (s, 3H), 1.51 (dt, 1H, *J*=13.0, 11.6 Hz), 1.29 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 171.00, 101.84, 81.30, 70.83, 68.61, 57.46, 39.55, 38.72, 21.60, 21.11.

5.1.25. Hydroxy mesylate (−)-44β. A solution of mesylate (−)-**43**β (0.56 g, 2.0 mmol) in MeOH (20 mL) was treated with MeONa (0.020 g) and the reaction mixture was stirred 1 h at rt. Evaporation of the neutralized (10% aqueous HCl) organic solution afforded a crude solid reaction product (0.44 g) which was recrystallized from hexane/AcOEt to give pure *(−)-methyl 2-(O-mesyl)-4,6-dideoxy-β-D-glucopyranoside* (**44**β) (0.33 g, 69% yield), as a solid, mp 96–98°C (Found: C, 40.31; H, 6.38. $C_8H_{16}O_6S$ requires C, 39.99; H, 6.71): $[\alpha]_D^{25}$=−48.8 (*c* 3.0, $CHCl_3$). IR 3465 cm^{-1}(OH); ^1H NMR δ 4.30 (d, 1H, *J*=7.9 Hz), 4.15 (dd, 1H, *J*=8.9, 7.9 Hz), 3.78 (ddd, 1H, *J*=11.5, 8.9, 5.3 Hz), 3.62 (dqd, 1H, *J*=11.5, 6.2, 1.9 Hz), 3.54 (s, 3H), 3.14 (s, 3H), 2.10 (ddd, 1H, *J*=13.2, 5.3, 1.9 Hz), 1.50 (dt, 1H, *J*=13.2, 11.5 Hz), 1.29 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 101.54, 85.57, 69.89, 68.71, 57.43, 41.11, 39.12, 21.18.

5.1.26. Epoxide (−)-5. A solution of hydroxy mesylate (−)-**44**β (0.26 g, 1.08 mmol) in anhydrous benzene (6 mL) was treated with *t*-BuOK (0.24 g, 2.16 mmol) and the reaction mixture was stirred at rt for 30 min. Evaporation of the filtered organic solution afforded pure *(−)-methyl*

2,3-anhydro-4,6-dideoxy-β-D-mannopyranoside (**5**)[21] (0.143 g, 92% yield), as a liquid (Found: C, 58.63; H, 8.70. $C_7H_{12}O_3$ requires C, 58.32; H, 8.39): $[\alpha]_D^{25}=-95.2$ (*c* 1.7, $CHCl_3$); ^1H NMR δ 4.70 (s, 1H), 3.40–3.60 (m, 1H), 3.49 (s, 3H), 3.26 (td, 1H, *J*=4.5, 0.9 Hz), 3.02 (d, 1H, *J*=4.5 Hz), 1.79 (dt, 1H, *J*=15.2, 4.8 Hz), 1.66 (unresolved ddd, 1H, *J*=15.2, 10.8 Hz), 1.13 (d, 3H, *J*=6.1 Hz); ^{13}C NMR δ 99.49, 69.45, 56.98, 51.81, 50.34, 30.84, 21.43.

5.1.27. Epoxide (−)-6. Proceeding as previously described for the corresponding reaction of diol (+)-**31**α, the treatment of a solution of diol (−)-**31β** (0.116 g, 0.716 mmol) in anhydrous benzene (3 mL) containing 4 Å molecular sieves with PPh_3 (0.213 g, 0.81 mmol) and DEAD (0.14 g, 0.81 mmol) afforded a crude liquid product which was distilled (Kügel–Rohr) to give pure *(−)-methyl 2,3-anhydro-4,6-dideoxy-β-D-allopyranoside* (**6**)[21] (0.032 g, 31% yield), as a liquid, bp 130°C (13 mmHg) (Found: C, 58.51; H, 8.14. $C_7H_{12}O_3$ requires C, 58.32; H, 8.39): $[\alpha]_D^{25}=-83.0$ (*c* 0.9, $CHCl_3$); ^1H NMR δ 4.61 (s, 1H), 3.48 (s, 3H), 3.36–3.52 (m, 1H), 3.24–3.31 (m, 1H), 3.06 (d, 1H, *J*=4.0 Hz), 1.97 (dt, 1H, *J*=14.7, 2.4 Hz), 1.63 (ddd, 1H, *J*=14.7, 10.8, 1.7 Hz), 1.12 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 99.63, 63.02, 57.18, 54.01, 52.07, 33.10, 21.46.

5.1.28. Glycal (±)-48. A suspension of NaH (2.0 g of a 60% dispersion in mineral oil, 50.0 mmol) in anhydrous DMF (20 mL) was treated at 0°C under stirring with a solution of alcohol (±)-**47**[23] (2.92 g, 24.96 mmol) in anhydrous DMF (46 mL). The reaction mixture was stirred for 1 h at rt, then, after cooling at 0°C, BnBr (4.28 g, 25.0 mmol) was added and the reaction mixture was stirred at rt for 24 h. After cooling at 0°C, ice was added and the reaction mixture was extracted with ether. Evaporation of the washed (water) organic extracts afforded a crude product (4.80 g) consisting of benzyl derivative **48** which was subjected to flash chromatography. Elution with an 1:1 hexane/CH_2Cl_2 mixture afforded pure *(±)-cis-4-benzyloxy-3,4-dihydro-2-methyl-2H-pyran* (**48**) (2.50 g, 49% yield) (Found: C, 76.21; H, 8.10. $C_{13}H_{16}O_2$ requires C, 76.44; H, 7.90); ^1H NMR δ 7.04–7.34 (m, 5H), 6.30 (dd, 1H, *J*=6.3, 1.9 Hz), 4.76 (dt, 1H, *J*=6.3, 1.9 Hz), 4.46 (s, 2H), 4.13 (ddt, 1H, *J*=9.2, 6.5, 1.9 Hz), 3.95 (dqd, 1H, *J*=11.1, 6.4, 1.9 Hz), 2.05 (ddt, 1H, *J*=13.0, 6.3, 1.9 Hz), 1.63 (ddd, 1H, *J*=13.0, 11.2, 9.2 Hz), 1.22 (d, 3H, *J*=6.4 Hz); ^{13}C NMR δ 146.08, 139.24, 128.96, 128.17, 128.08, 103.00, 71.64, 70.36, 70.05, 36.78, 21.59.

5.1.29. Reaction of glycal (±)-48 with DMDO. A solution of glycal (±)-**48** (0.30 g, 1.47 mmol) in MeOH (20 mL) was treated under stirring at 0°C with solid $NaHCO_3$ (0.37 g, 4.41 mmol), oxone® (0.90 g, 1.47 mmol), a catalytic amount of EDTA and acetone (1.6 mL). After 2 days stirring at the same temperature, evaporation of the filtered organic solvent afforded a residue which was taken up with Et_2O. Evaporation of the washed (10% aqueous $Na_2S_2O_3$) organic solution afforded a crude reaction product consisting of a 9:1 mixture of glycosides (±)-**50**β and (±)-**50**α (0.29 g, 78% yield) which turned out to be not separable under any chromatographic conditions tried.

(±)-**50**β: ^1H NMR δ 7.16–7.32 (m, 5H), 4.64 (d, 1H, *J*=11.8 Hz), 4.56 (d, 1H, *J*=11.8 Hz), 4.06 (d, 1H, *J*=7.3 Hz), 3.22–3.58 (m, 3H), 3.48 (s, 3H), 1.98 (ddd, 1H, *J*=12.9, 4.6, 2.0 Hz), 1.33 (dt, 1H, *J*=12.9, 11.7 Hz), 1.20 (d, 3H, *J*=6.2 Hz); ^{13}C NMR: δ 139.11, 129.15, 128.42, 104.51, 78.87, 75.66, 72.26, 68.73, 57.59, 38.64, 21.63 (1×Ph signal unresolved).

(±)-**50**α: ^1H NMR δ 4.70 (d, 1H, *J*=3.5 Hz), 1.14 (d, 3H, *J*=6.3 Hz).

5.1.30. Acetates (±)-51α and (±)-51β. A solution of the 9:1 mixture of alcohols (±)-**50**β and (±)-**50**α (0.177 g, 0.70 mmol) in anhydrous pyridine (3 mL) was treated under stirring at rt with Ac_2O (0.5 mL). After 1 h, the usual treatment afforded a crude product consisting of a 9:1 mixture of acetates (±)-**51**β and (±)-**51**α (0.19 g, 92% yield), which was directly utilized in the next step.

(±)-**51**β, a liquid. IR 1745 cm^{-1} (CO); ^1H NMR δ 7.16–7.32 (m, 5H), 4.80 (dd, 1H, *J*=9.3, 8.0 Hz), 4.57 (d, 1H, *J*=12.2 Hz), 4.41 (d, 1H, *J*=12.2 Hz), 4.15 (d, 1H, *J*=8.0 Hz), 3.32–3.58 (m, 2H), 3.39 (s, 3H), 2.02 (ddd, 1H, *J*=12.9, 5.3, 1.7 Hz), 2.00 (s, 3H), 1.41 (dt, 1H, *J*=12.9, 11.5 Hz), 1.22 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 170.53, 139.96, 129.03, 128.31, 128.10, 102.55, 77.08, 74.62, 71.62, 68.62, 57.01, 38.76, 21.78, 21.55.

5.1.31. Hydroxy acetate (±)-34β. A solution of the 9:1 mixture of acetates (±)-**51**β and (±)-**51**α (0.22 g, 0.75 mmol) in MeOH (3 mL) was stirred under a hydrogen atmosphere in the presence of Pd/C (0.020 g). After 24 h, evaporation of the filtered organic solution afforded a crude product consisting of *(±)-methyl 2-(O-acetyl)-4,6-dideoxy-β-D-glucopyranoside* (**34β**) (0.13 g, 85% yield), as a liquid (Found: C, 52.81; H, 7.64. $C_9H_{16}O_5$ requires C, 52.93; H, 7.90). IR 1746 cm^{-1} (CO); ^1H NMR δ 4.53 (dd, 1H, *J*=9.3, 7.9 Hz), 4.17 (d, 1H, *J*=7.9 Hz), 3.66 (ddd, 1H, *J*=11.5, 9.3, 5.2 Hz), 3.52 (dqd, 1H, *J*=11.5, 6.2, 1.9 Hz), 3.40 (s, 3H), 2.06 (s, 3H), 1.98 (ddd, 1H, *J*=13.0, 5.2, 1.9 Hz), 1.40 (dt, 1H, *J*=13.0, 11.5 Hz), 1.21 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 170.06, 102.18, 77.08, 70.64, 68.54, 57.07, 41.59, 21.67, 21.26.

5.1.32. Mesylate (±)-35β. A solution of hydroxy acetate (±)-**34**β (0.13 g, 0.64 mmol) in anhydrous pyridine (4 mL) was treated under stirring at 0°C with MsCl (2.96 g, 2.56 mmol). After 18 h stirring at rt, dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic solution afforded a crude solid product (0.18 g) which was recrystallized fom hexane/acetone to give pure *(±)-methyl 2-(O-acetyl)-3-(O-mesyl)-4,6-dideoxy-β-D-glucopyranoside* (**35β**), as a solid, mp 108–110°C (0.13 g, 72% yield) (Found: C, 42.21; H, 6.18. $C_{10}H_{18}O_7S$ requires C, 42.55; H, 6.43). IR 1747 cm^{-1} (CO); ^1H NMR δ 4.85 (dd, 1H, *J*=9.4, 7.5 Hz), 4.72 (ddd, 1H, *J*=11.5, 9.5, 5.2 Hz), 4.26 (d, 1H, *J*=7.6 Hz), 3.59 (dqd, 1H, *J*=11.5, 6.2, 1.9 Hz), 3.45 (s, 3H), 2.97 (s, 3H), 2.22 (ddd, 1H, *J*=12.9, 5.2, 1.9 Hz), 2.08 (s, 3H), 1.70 (dt, 1H, *J*=12.9, 11.5 Hz), 1.28 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 169.95, 101.83, 77.72, 72.17, 67.64, 56.99, 39.57, 38.91, 21.21, 20.83.

5.1.33. Epoxide (±)-6. Following the usual procedure, the treatment of a solution of mesylate (±)-**35**β (0.14 g, 0.49 mmol) in MeOH (1 mL) with MeONa (0.010 g)

afforded, after 24 h stirring at rt, a crude product which was dissolved in anhydrous benzene (3 mL) and treated with *t*-BuOK (0.102 g, 0.90 mmol). After 30 min stirring at rt, evaporation of the filtered organic solution afforded pure epoxide (±)-**6**,[21] as a liquid (0.049 g, 69% yield).

5.1.34. Mesylates (±)-52β and 52α. A solution of the 9:1 mixture of alcohols (±)-**50**β and (±)-**50**α (0.204 g, 0.81 mmol) in anhydrous pyridine (5 mL) was treated at 0°C with MsCl (3.72 g, 3.25 mmol). After 3 h, dilution with CH_2Cl_2 and evaporation of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic solution afforded a crude product consisting of a 9:1 mixture of mesylates (±)-**52**β and (±)-**52**α (0.25 g, 93% yield).

(±)-**52**β: ^{1}H NMR δ 7.10–7.34 (m, 5H), 4.60 (d, *J*=11.8 Hz), 4.53 (d, *J*=11.8 Hz), 4.27 (t, 1H, *J*=8.3 Hz), 4.19 (d, 1H, *J*=8.3 Hz), 3.56 (ddd, 1H, *J*=11.5, 8.3, 5.3 Hz), 3.37–3.54 (m, 1H), 3.44 (s, 3H), 2.95 (s, 3H), 2.05 (ddd, 1H, *J*=13.0, 5.3, 1.8 Hz), 1.37 (dt, 1H, *J*=13.0, 11.5 Hz), 1.19 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 138.25, 128.95, 128.43, 128.35, 101.90, 83.55, 76.49, 72.15, 68.46, 57.24, 39.58, 38.94, 21.18.

(±)-**52**α: ^{1}H NMR δ 7.15–7.34 (m, 5H), 4.82 (d, 1H, *J*=3.6 Hz), 4.58 (d, *J*=11.3 Hz), 4.44 (d, *J*=11.3 Hz), 4.37 (dd, 1H, *J*=9.8, 3.6 Hz), 3.90 (ddd, 1H, *J*=11.1, 9.8, 5.2 Hz), 3.72–3.90 (m, 1H), 3.34 (s, 3H), 2.90 (s, 3H), 2.13 (ddd, 1H, *J*=12.8, 5.2, 2.2 Hz), 1.35 (dt, 1H, *J*=12.8, 11.5 Hz), 1.14 (d, 3H, *J*=6.2 Hz).

5.1.35. Hydroxy mesylate (±)-44β. A solution of the 9:1 mixture of mesylates (±)-**52**β and (±)-**52**α (0.165 g, 0.50 mmol) in MeOH (2 mL) was hydrogenated at rt in the presence of Pd/C (0.014 g). After 24 h, the usual work-up afforded a crude solid product (0.115 g) consisting of the hydroxy mesylate (±)-**44**β (^{1}H and ^{13}C NMR), which was recrystallized from hexane/AcOEt to give pure (±)-**44**β, as a solid, mp 75.5–77.5°C (0.098 g, 82% yield).

5.1.36. Epoxide (±)-5. Following the usual procedure, the treatment of a solution of hydroxy mesylate (±)-**44**β (0.11 g, 0.46 mmol) in anhydrous benzene (3 mL) with *t*-BuOK (0.102 g, 0.90 mmol) afforded pure epoxide (±)-**5** (^{1}H and ^{13}C NMR),[21] as a liquid (0.045 g, 68% yield).

5.1.37. Diels–Alder reaction between Danishefsky diene and acetaldehyde. Following a previously described procedure,[25b] a 25 mL oven-dried schlenk was charged with (*R*,*R*)-(salen)Cr(III)–OTf complex (0.030 g, 0.042 mmol)[25a] and oven-dried powdered 4 Å molecular sieves (0.60 g). The schlenk was sealed with a rubber septum and purged with argon. The catalyst was dissolved in TBME (0.5 mL), and acetaldehyde (0.11 mL, 2.06 mmol) was added via syringe at rt. The reaction mixture was then cooled to −30°C followed by addition of diene **45** (Danishefsky diene) (0.4 mL, 2.05 mmol). After 24 h stirring at the same temperature, the reaction mixture was diluted with CH_2Cl_2 (5 mL) and treated with two drops of TFA. After 15 min stirring at rt, the reaction mixture was concentrated in vacuo and the crude residue was subjected to flash chromatography. Elution with a 7:3 hexane/AcOEt mixture afforded pure enone **46** (0.19 g, 82% yield), as a clear liquid, which turned out to be 57% ee, as determined by chiral GC analysis on a CP-Cyclodex-B fused silica capillary column (50 m×0.25 mm) (Chrompack): low isotherm 80°C, high isotherm 120°C, increasing temperature 4°C/min.

5.2. Azidolysis of epoxides 3–8 with NaN_3–NH_4Cl

General procedure. A solution of the epoxide (0.50 mmol) in an 8:1 MeOH/H_2O mixture (3.0 mL) was treated with NaN_3 (0.160 g, 2.46 mmol) and NH_4Cl (0.060 g, 1.12 mmol) and the resulting reaction mixture was stirred at 80°C for the time shown in Tables 1 and 2. Evaporation of the organic solvent afforded a crude product which was filtered through a silica gel pad (a 7:3 hexane/AcOEt mixture was used as the eluant) to give a crude reaction mixture which was analyzed by ^{1}H NMR (Tables 1 and 2). In the case of epoxides **3** and **4**, the reaction mixture was diluted with ether, and the organic solution washed (water) and evaporated.

The crude reaction mixture of azido alcohols from epoxide **8** (0.084 g) was subjected to TLC (a 95:5 CH_2Cl_2/AcOEt mixture was used as the eluant). Extraction of the most intense bands afforded the corresponding C-2 (0.015 g, 16% yield) and *C-3 product* (0.055 g, 59% yield).

(+)-Methyl 2-(azido)-2,4,6-trideoxy-α-D-altropyranoside (***C-2 product***), a liquid (Found: C, 44.74; H, 6.69; N, 22.30. $C_7H_{13}N_3O_3$ requires C, 44.91; H, 7.00; N, 22.45): $[\alpha]_D^{25}$=+40.5 (*c* 0.6, $CHCl_3$); ^{1}H NMR δ 4.72–4.80 (br s, 1H), 4.02–4.20 (m, 1H), 3.86–4.02 (m, 1H), 3.45–3.55 (m, 1H), 3.44 (s, 3H), 1.65–1.88 (m, 2H), 1.25 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 100.35, 67.36, 60.60, 59.60, 56.27, 36.08, 21.54.

(+)-Methyl 3-(β-azido)-3,4,6-trideoxy-α-D-glucopyranoside (***C-3 product***), a liquid (Found: C, 44.88; H, 6.93; N, 22.12. $C_7H_{13}N_3O_3$ requires C, 44.91; H, 7.00; N, 22.45): $[\alpha]_D^{25}$=+199.6 (*c* 1.2, $CHCl_3$); ^{1}H NMR δ 4.74 (d, 1H, *J*=3.7 Hz), 3.90 (dqd, 1H, *J*=11.7, 6.3, 2.1 Hz), 3.67 (ddd, 1H, *J*=11.7, 9.9, 4.6 Hz), 3.50 (dd, 1H *J*=9.9, 3.7 Hz), 3.36 (s, 3H), 1.95 (ddd, 1H, *J*=13.1, 4.6, 2.1 Hz), 1.34 (dt, 1H, *J*=13.1, 11.7 Hz), 1.21 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 99.29, 72.61, 63.60, 60.04, 55.17, 37.52, 20.57.

The crude reaction product (0.092 g) from epoxide **7** was subjected to flash cromatography. Elution with an 85:15 hexane/AcOEt mixture afforded pure *(+)-methyl 3-(azido)-3,4,6-trideoxy-α-D-altropyranoside* (***C-3 product***) (0.082 g, 88% yield), as a liquid (Found: C, 45.20; H, 7.19; N, 22.54. $C_7H_{13}N_3O_3$ requires C, 44.91; H, 7.00; N, 22.45): $[\alpha]_D^{25}$=+81.3 (*c* 3.0, $CHCl_3$); ^{1}H NMR δ 4.56 (d, 1H, *J*=3.4 Hz), 4.15 (dqd, 1H, *J*=8.2, 6.4, 3.8 Hz), 3.77 (q, 1H, *J*=5.2 Hz), 3.57 (dd, 1H, *J*=5.1, 3.4 Hz), 3.44 (s, 3H), 1.86 (ddd, 1H, *J*=14.1, 8.2, 5.1 Hz), 1.67 (ddd, 1H, *J*=14.1, 5.1, 3.8 Hz), 1.25 (d, 3H, *J*=6.4 Hz); ^{13}C NMR δ 101.51, 69.80, 62.93, 58.60, 56.52, 33.27, 20.77.

The azido alcohols present in the crude reaction mixture (0.086 g) from epoxide **6** turned out to be not separable by TLC. Recrystallization of the crude product from hexane/AcOEt afforded pure *(+)-methyl*

3-(azido)-3,4,6-trideoxy-β-D-glucopyranoside (***C-3 product***) (0.020 g, 21% yield), as a solid, mp 138.5–139.5°C (Found: C, 45.08; H, 7.26; N, 22.68. $C_7H_{13}N_3O_3$ requires C, 44.91; H, 7.00; N, 22.45): $[\alpha]_D^{25}=+27.5$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 4.11 (d, 1H, *J*=7.5 Hz), 3.60 (dqd, 1H, *J*=11.7, 6.2, 2.0 Hz), 3.52 (s, 3H), 3.48 (ddd, 1H, *J*=11.7, 9.6, 5.0 Hz), 3.29 (dd, *J*=9.6, 7.5 Hz), 1.94 (ddd, 1H, *J*=13.2, 5.0, 2.0 Hz), 1.38 (dt, 1H, *J*=13.2, 11.7 Hz), 1.26 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 104.64, 75.04, 69.29, 62.07, 57.75, 38.37, 21.42.

C-2 product. ^{1}H NMR δ 4.83 (d, 1H, *J*=1.7 Hz), 3.99 (dqd, 1H, *J*=10.0, 6.4, 3.1 Hz), 3.55 (s, 3H), 3.44–3.50 (m, 1H), 1.72 (ddd, 1H, *J*=14.3, 10.0, 3.1 Hz), 1.38 (dt, 1H, *J*=14.2, 3.1 Hz), 1.28 (d, 3H, *J*=6.4 Hz).

The crude reaction product (0.091 g) from epoxide **5** was subjected to flash chromatography. Elution with a 98:2 CH_2Cl_2/MeOH mixture afforded pure *(+)-methyl 3-(azido)-3,4,6-trideoxy-β-D-altropyranoside* (***C-3 product***) (0.072 g, 77% yield), as a liquid (Found: C, 44.58; H, 6.65; N, 22.10. $C_7H_{13}N_3O_3$ requires C, 44.91; H, 7.00; N, 22.45): $[\alpha]_D^{25}=-134.4$ (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 4.49 (d, 1H, *J*=1.5 Hz), 3.90 (q, 1H, *J*=3.0 Hz), 3.80 (dqd, 1H, *J*=10.0, 6.3, 3.0 Hz), 3.51–3.56 (m, 1H), 3.46 (s, 3H), 1.55 (dt, 1H, *J*=14.0, 3.0 Hz), 1.67 (ddd, 1H, *J*=14.0, 5.7, 3.0 Hz), 1.21 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 99.59, 68.26, 67.68, 59.84, 56.91, 32.53, 21.57.

The crude reaction product (0.13 g) from epoxide **4** was subjected to preparative TLC (a 7:3 hexane/AcOEt mixture was used as the eluant). Extraction of the two most intense bands afforded the corresponding C-3 (0.079 g, 60% yield) and *C-4 product* (0.012 g, 9% yield).

(+)-Benzyl 3-(azido)-2,3,6-trideoxy-α-D-glucopyranoside (***C-3 product***), a liquid (Found: C, 59.65; H, 6.34; N, 15.69. $C_{13}H_{17}N_3O_3$ requires C, 59.30; H, 6.51; N, 15.96): $[\alpha]_D^{25}=+110.4$ (*c* 1.9, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 4.95 (unresolved dd, 1H, *J*=3.0 Hz), 4.68 (d, 1H, *J*=11.8 Hz), 4.46 (d, 1H, *J*=11.8 Hz), 3.65–3.90 (m, 2H), 3.15 (t, 1H, *J*=9.4 Hz), 2.20 (ddd, 1H, *J*=13.1, 4.9, 1.0 Hz), 1.73 (td, 1H, *J*=12.6, 3.5 Hz), 1.30 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 138.02, 129.13, 128.58, 96.28, 76.70, 69.60, 68.49, 61.05, 35.57, 18.39 (1×Ph signal unresolved).

(+)-Benzyl 4-(azido)-2,4,6-trideoxy-α-D-gulopyranoside (***C-4 product***), a liquid (Found: C, 59.26; H, 6.44; N, 15.73. $C_{13}H_{17}N_3O_3$ requires C, 59.30; H, 6.51; N, 15.96): $[\alpha]_D^{25}=+123.4$ (*c* 1.1, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 5.01 (unresolved dd, 1H, *J*=3.5 Hz), 4.70 (d, 1H, *J*=11.8 Hz), 4.50 (d, 1H, *J*=11.8 Hz), 4.33 (dq, 1H, *J*=6.5, 1.7 Hz), 3.97–4.10 (m, 1H), 3.31–3.40 (m, 1H), 2.11 (dt, 1H, *J*=14.8, 3.5 Hz), 1.88 (ddd, 1H, *J*=14.7, 2.7, 1.2 Hz), 1.30 (d, 3H, *J*=6.5 Hz); ^{13}C NMR δ 137.47, 129.24, 128.76, 128.64, 97.75, 70.40, 67.15, 64.45, 61.57, 30.95, 18.04.

The crude reaction product (0.127 g) from epoxide **3** was subjected to preparative TLC (a 7:3 hexane/AcOEt mixture was used as the eluant). Extraction of the two most intense bands afforded the corresponding C-3 (0.095 g, 72% yield) and *C-4 product* (0.007 g, 5% yield).

(+)-Benzyl 3-(azido)-2,3,6-trideoxy-α-D-gulopyranoside (***C-3 product***), a liquid (Found: C, 59.55; H, 6.72; N, 15.88. $C_{13}H_{17}N_3O_3$ requires C, 59.30; H, 6.51; N, 15.96): $[\alpha]_D^{25}=+220.4$ (*c* 1.3, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 4.89 (unresolved dd, 1H, *J*=4.1 Hz), 4.75 (d, 1H, *J*=12.4 Hz), 4.52 (d, 1H, *J*=12.4 Hz), 4.28 (dq, 1H, *J*=6.7, 1.1 Hz), 3.83 (dd, 1H, *J*=7.2, 3.8 Hz), 3.30–3.41 (m, 1H), 2.16 (dt, 1H, *J*=15.2, 4.4 Hz), 1.82–1.92 (m, 1H), 1.17 (d, 3H, *J*=6.7 Hz); ^{13}C NMR δ 138.46, 129.02, 128.20, 128.12, 95.72, 69.81, 62.71, 57.97, 27.61, 16.90 (1×*C*H signals unresolved). Acetate, a solid, mp 41–42.5°C (recrystallized from hexane): $[\alpha]_D^{25}=+183.5$ (*c* 1.3, $CHCl_3$); ^{1}H NMR δ 7.20–7.41 (m, 5H), 4.80 (dd, 1H, *J*=4.1, 1.4 Hz), 4.75 (d, 1H, *J*=12.4 Hz), 4.53 (d, 1H, *J*=12.4 Hz), 4.61 (dd, 1H, *J*=3.8, 1.5 Hz), 4.30 (dq, 1H, *J*=6.7, 1.6 Hz), 3.87 (q, 1H, *J*=3.8 Hz), 2.13 (s, 3H), 2.08–2.22 (m, 1H), 1.89–2.02 (m, 1H), 1.10 (d, 3H, *J*=6.7 Hz); ^{13}C NMR δ 170.89, 138.40, 128.99, 128.15, 95.49, 70.74, 69.86, 61.75, 55.24, 28.24, 21.48, 16.85 (1×Ph signal unresolved).

(+)-Benzyl 4-(azido)-2,4,6-trideoxy-α-D-glucopyranoside (***C-4 product***), a solid, mp 71.5–72.5°C (recrystallized from hexane) (Found: C, 59.14; H, 6.41; N, 15.67. $C_{13}H_{17}N_3O_3$ requires C, 59.30; H, 6.51; N, 15.96): $[\alpha]_D^{25}=+110.9$ (*c* 0.8, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 4.97 (dd, 1H, *J*=3.6, 1.0 Hz), 4.65 (d, 1H, *J*=11.9 Hz), 4.44 (d, 1H, *J*=11.9 Hz), 4.01 (ddd, 1H, *J*=11.6, 9.6, 5.1 Hz), 3.67 (dq, 1H, *J*=9.6, 6.2 Hz), 2.96 (t, 1H, *J*=9.7 Hz), 2.19 (ddd, 1H, *J*=13.1, 5.1, 1.0 Hz), 1.73 (ddd, 1H, *J*=13.1, 11.6, 3.6 Hz), 1.33 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 138.18, 129.17, 128.51, 97.17, 71.44, 69.71, 68.61, 67.40, 38.47, 19.23 (1×Ph signal unresolved).

5.2.1. Azidolysis of epoxides 3–8 with NaN_3–$LiClO_4$. *General procedure*. A solution of the epoxide (0.50 mmol) in anhydrous CH_3CN (1.0 mL) was treated with NaN_3 (0.045 g, 0.70 mmol) and anhydrous $LiClO_4$ (0.266 g, 2.5 mmol) and the reaction mixture was stirred at 80°C for the time shown in Tables 1 and 2. Evaporation of the organic solvent afforded a crude product which was filtered through a silica gel pad (a 7:3 hexane/AcOEt mixture was used as the eluant) to give a crude reaction mixture which was analyzed by ^{1}H NMR (Tables 1 and 2). In the case of epoxides **3** and **4**, the reaction mixture was diluted with ether, and the organic solution washed (water) and evaporated.

5.2.2. Methanolysis of epoxides 3–8 with MeONa in anhydrous MeOH. *General procedure*. A solution of the epoxide (0.50 mmol) in a freshly prepared 2 M MeONa in anhydrous MeOH (2 mL) was stirred at 80°C for the time shown in Tables 1 and 2. Evaporation of the neutralized (10% aqueous HCl) organic solution afforded a crude product which was analyzed by ^{1}H NMR (Tables 1 and 2).

The crude reaction mixture (0.084 g) of methoxy alcohols from epoxide **8** was subjected to preparative TLC (a 7:3 hexane/AcOEt mixture was used as the eluant). Extraction of the two most intense bands afforded the corresponding pure C-2 (0.015 g, 17% yield) and *C-3 product* (0.045 g, 51% yield).

(+)-Methyl 2-(O-methyl)-4,6-dideoxy-α-D-altropyranoside (***C-2 product***), a liquid (Found: C, 54.36; H, 9.28. $C_8H_{16}O_4$ requires C, 54.53; H, 9.15): $[\alpha]_D^{25}$=+81.8 (*c* 1.1, $CHCl_3$) [lit.[11] $[\alpha]_D^{18}$=+85.5 (*c* 1.82, $CHCl_3$); lit.[11b] $[\alpha]_D^{21}$=+82.4 (*c* 1.5, $CHCl_3$)]. Acetate, a liquid: $[\alpha]_D^{25}$=+84.5 (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 4.99 (q, 1H, *J*=3.2 Hz), 4.65 (br s, 1H), 4.00 (dqd, 1H, *J*=10.7, 6.4, 3.2 Hz), 3.47 (s, 3H), 3.38 (s, 3H), 3.15–3.21 (m, 1H), 2.08 (s, 3H), 1.83 (ddd, 1H, *J*=14.3, 10.7, 3.2 Hz), 1.60 (ddd, 1H, *J*=14.3, 3.2, 2.6 Hz), 1.20 (d, 3H, *J*=6.4 Hz); ^{13}C NMR δ 171.18, 100.25, 75.24, 67.88, 60.49, 59.02, 55.72, 33.23, 21.85, 21.47.

(+)-Methyl 3-(O-methyl)-4,6-dideoxy-α-D-glucopyranoside (***C-3 product***), a liquid (Found: C, 54.17; H, 9.03. $C_8H_{16}O_4$ requires C, 54.53; H, 9.15): $[\alpha]_D^{25}$=+188.6 (*c* 1.6, $CHCl_3$) [lit.[11a] $[\alpha]_D^{18}$=+192.6 (*c* 1.27, $CHCl_3$); lit.[11b] $[\alpha]_D^{23}$=+192 (*c* 1.2, $CHCl_3$)]. Acetate, a liquid: $[\alpha]_D^{25}$=+166.2 (*c* 2.0, $CHCl_3$); ^{1}H NMR δ 4.85 (d, 1H, *J*=3.7 Hz), 4.75 (dd, 1H, *J*=9.8, 3.7 Hz), 3.91 (dqd, 1H, *J*=11.6, 6.3, 2.2 Hz), 3.67 (ddd, 1H, *J*=11.6, 9.8, 5.0 Hz), 3.44 (s, 3H), 3.38 (s, 3H), 3.37 (s, 3H), 2.15 (ddd, 1H, *J*=12.7, 5.0, 2.2 Hz), 1.34 (dt, 1H, *J*=12.7, 11.6 Hz), 1.22 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 171.26, 98.29, 75.04, 74.98, 64.10, 57.90, 55.66, 38.69, 21.85, 21.54.

The crude reaction product (0.087 g) from epoxide **7** was subjected to flash cromatography. Elution with an 1:1 hexane/AcOEt mixture afforded pure *methyl 3-(O-methyl)-4,6-dideoxy-α-D-altropyranoside* (***C-3 product***) (0.078 g, 88% yield), as a liquid (Found: C, 54.78; H, 9.41. $C_8H_{16}O_4$ requires C, 54.53; H, 9.15): $[\alpha]_D^{25}$=+82.4 (*c* 1.2, $CHCl_3$) [lit.[11b] $[\alpha]_D^{23}$=+83.4 (*c* 1.8, $CHCl_3$)]. Acetate, a liquid: $[\alpha]_D^{25}$=+75.4 (*c* 1.1, $CHCl_3$); ^{1}H NMR δ 4.81–4.88 (m, 1H), 4.60 (broad s, 1H), 4.07–4.13 (dqd, 1H, *J*=9.7, 6.4, 3.5 Hz), 3.35–3.57 (m, 1H), 3.44 (s, 3H), 3.40 (s, 3H), 2.10 (s, 3H), 1.58–1.82 (m, 2H), 1.21 (d, 3H, *J*=6.4 Hz); ^{13}C NMR δ 170.55, 100.18, 75.40, 67.00, 60.27, 58.05, 56.31, 33.59, 21.81 (1×Me signals unresolved).

The methoxy alcohols contained in the crude reaction mixture (0.086 g) from epoxide **6** turned out to be not separable by TLC. Acetylation afforded a crude reaction product (0.092 g, 84% yield) which was analyzed by ^{1}H NMR.

C-2 product. ^{1}H NMR δ 5.09 (q, 1H, *J*=3.2 Hz), 4.48 (d, 1H, *J*=1.2 Hz), 3.77 (dqd, 1H, *J*=11.1, 6.3, 2.6 Hz), 3.15 (dd, 1H, *J*=3.2, 1.2 Hz), 2.03 (s, 3H), 1.72 (ddd, 1H, *J*=14.5, 11.1, 3.2 Hz), 1.52 (dt, 1H, *J*=14.5, 2.6 Hz), 1.18 (d, 3H, *J*=6.3 Hz).

C-3 product. ^{1}H NMR δ 4.70 (dd, 1H, *J*=9.3, 8.0 Hz), 4.17 (d, 1H, *J*=8.0 Hz), 2.03 (s, 3H), 1.31 (dt, 1H, *J*=12.8, 11.6 Hz), 1.22 (d, 3H, *J*=6.3 Hz).

The crude reaction product (0.062 g, 70% yield) from epoxide **5** turned out to be consisting of practically pure *(−)-methyl 3-(O-methyl)-4,6-dideoxy-β-D-altropyranoside* (***C-3 product***), as a liquid (Found: C, 54.82; H, 9.39. $C_8H_{16}O_4$ requires C, 54.53; H, 9.15): $[\alpha]_D^{25}$=−67.6 (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 4.51 (d, 1H, *J*=1.3 Hz), 3.79 (sextet, 1H, *J*=6.3 Hz), 3.61 (dd, 1H, *J*=3.5, 1.3 Hz), 3.51 (q, 1H *J*=3.5 Hz), 3.46 (s, 3H), 3.32 (s, 3H), 1.59 (dd, 1H, *J*=7.3, 2.9 Hz), 1.59 (dd, 1H, *J*=6.0, 2.9 Hz), 1.17 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 100.15, 78.16, 67.53, 67.45, 57.66, 56.99, 32.71, 21.81.

The crude reaction mixture (0.11 g) from epoxide **3** was subjected to preparative TLC (a 7:3 hexane /AcOEt was used as the eluant). Extraction of the two most intense bands afforded the corresponding C-3 (0.075 g, 60% yield) and *C-4 product* (0.017 g, 13% yield).

(+)-Benzyl 2,6-dideoxy-3-(O-methyl)-α-D-gulopyranoside (***C-3 product***), a liquid (Found: C, 66.39; H, 7.68. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99): $[\alpha]_D^{25}$=+139.7 (*c* 1.3, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 4.83 (dd, 1H, *J*=4.2, 2.1 Hz), 4.75 (d, 1H, *J*=12.5 Hz), 4.52 (d, 1H, *J*=12.5 Hz), 4.33 (q, 1H, *J*=6.7 Hz), 3.37–3.60 (m, 2H), 3.42 (s, 3H), 1.84–2.10 (m, 2H), 1.18 (d, 3H, *J*=6.7 Hz); ^{13}C NMR δ 138.78, 128.96, 128.33, 128.09, 96.10, 77.11, 69.63, 69.53, 63.26, 57.55, 28.59, 16.83. Acetate, a liquid: $[\alpha]_D^{25}$=+128.4 (*c* 1.3, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 4.89 (t, 1H, *J*=3.3 Hz), 4.82 (dd, 1H, *J*=3.3, 1.3 Hz), 4.74 (d, 1H, *J*=12.5 Hz), 4.54 (d, 1H, *J*=12.5 Hz), 4.35 (dq, 1H, *J*=6.7, 1.3 Hz), 3.40–3.51 (m, 1H), 3.45 (s, 3H), 2.12 (s, 3H), 1.95 (t, 2H, *J*=3.3 Hz), 1.10 (d, 3H, *J*=6.7 Hz); ^{13}C NMR δ 171.21, 138.71, 128.93, 128.49, 128.09, 95.78, 74.35, 70.38, 69.53, 61.76, 57.86, 29.38, 21.63, 17.02.

(+)-Benzyl 2,6-dideoxy-4-O-methyl-α-D-glucopyranoside (***C-4 product***), a solid, mp 120.5–122.5°C (recrystallized from hexane) (Found: C, 66.57; H, 8.11. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99): $[\alpha]_D^{25}$=+132.2 (*c* 0.2, $CHCl_3$); ^{1}H NMR δ 7.20–7.41 (m, 5H), 4.93 (unresolved dd, 1H, *J*=3.4 Hz), 4.66 (d, 1H, *J*=11.9 Hz), 4.43 (d, 1H, *J*=11.9 Hz), 4.02 (ddd, 1H, *J*=11.6, 9.2, 5.4 Hz), 3.69 (dq, 1H, *J*=9.2, 6.3 Hz), 3.58 (s, 3H), 2.74 (t, 1H, *J*=9.2 Hz), 2.18 (ddd, 1H, *J*=12.8, 5.4, 1.0 Hz), 1.71 (ddd, 1H, *J*=12.8, 11.6, 3.7 Hz), 1.30 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 138.46, 129.08, 128.46, 128.34, 97.16, 88.79, 69.49, 69.38, 67.89, 61.60, 38.20, 18.87.

5.2.3. Methanolysis of epoxides 3–8 with MeOH–$LiClO_4$. *General procedure*. A solution of the epoxide (0.50 mmol) in anhydrous MeOH (2.0 mL) containing anhydrous $LiClO_4$ (3.60 g, 34.0 mmol) was stirred at 80°C for the time shown in Tables 1 and 2. After cooling, dilution with water, extraction with ether, and evaporation of the washed (saturated aqueous NaCl) ether extracts afforded a crude product which was analyzed by ^{1}H NMR (Tables 1 and 2). In the case of epoxides **5**–**8**, the crude product was filtered through a silica gel pad (an 1:1 hexane/AcOEt mixture was used as the eluant).

The crude product (0.11 g) from epoxide **4** was subjected to preparative TLC (an 1:1 hexane/AcOEt was used as the eluant). Extraction of the two most intense bands afforded the corresponding C-3 (0.008 g, 6% yield) and *C-4 product* (0.084 g, 67% yield):

(+)-Benzyl 2,6-dideoxy-4-(O-methyl)-α-D-gulopyranoside (***C-4 product***), a liquid (Found: C, 66.92; H, 7.60. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99): $[\alpha]_D^{25}$=+96.5 (*c*

1.2, $CHCl_3$); ^1H NMR δ 7.20–7.40 (m, 5H), 5.01 (unresolved dd, 1H, J=3.4 Hz), 4.72 (d, 1H, J=11.9 Hz), 4.52 (d, 1H, J=11.9 Hz), 4.25 (dq, 1H, J=6.5, 1.3 Hz), 3.97–4.10 (m, 1H), 3.46 (s, 3H), 2.98–3.04 (m, 1H), 2.14 (dt, 1H, J=14.6, 3.6 Hz), 1.84 (ddd, 1H, J=14.6, 2.8, 1.2 Hz), 1.27 (d, 3H, J=6.5 Hz); ^{13}C NMR δ 137.85, 129.16, 128.55, 98.06, 80.45, 70.15, 65.00, 62.32, 59.65, 31.00, 17.10 (1×Ph signal unresolved).

(+)-Benzyl 2,6-dideoxy-3-(O-methyl)-α-D-glucopyranoside (***C-3 product***), a liquid (Found: C, 66.47; H, 7.81. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99): $[\alpha]_D^{25}$=+107.4 (*c* 1.2, $CHCl_3$); ^1H NMR δ 7.20–7.40 (m, 5H), 4.99 (unresolved dd, 1H, J=3.1 Hz), 4.69 (d, 1H, J=11.9 Hz), 4.45 (d, 1H, J=11.9 Hz), 3.76 (dq, 1H, J=9.1, 6.3 Hz), 3.57 (ddd, 1H, J=11.4, 9.1, 4.9 Hz), 3.39 (s, 3H), 3.19 (td, 1H, J=9.1, 1.7 Hz), 2.58 (d, 1H (OH), J=1.7 Hz), 2.32 (ddd, 1H, J=12.8, 4.9, 1.1 Hz), 1.53 (ddd, 1H, J=12.8, 11.4, 3.7 Hz), 1.31 (d, 3H, J=6.3 Hz); ^{13}C NMR δ 138.34, 129.05, 128.58, 128.37, 97.23, 78.95, 76.72, 69.42, 68.31, 57.11, 34.55, 18.52. Acetate, a liquid: $[\alpha]_D^{25}$=+95.5 (*c* 1.2, $CHCl_3$); ^1H NMR δ 7.20–7.40 (m, 5H), 4.99 (unresolved dd, 1H, J=3.1 Hz), 4.70 (t, 1H, J=9.2 Hz), 4.67 (d, 1H, J=12.0 Hz), 4.46 (d, 1H, J=12.0 Hz), 3.82 (dq, 1H, J=9.2, 6.3 Hz), 3.68 (ddd, 1H, J=11.3, 9.2, 5.0 Hz), 3.33 (s, 3H), 2.32 (ddd, 1H, J=13.0, 5.0, 1.0 Hz), 2.10 (s, 3H), 1.66 (ddd, 1H, J=13.0, 11.3, 3.7 Hz), 1.16 (d, 3H, J=6.3 Hz); ^{13}C NMR δ 170.93, 138.26, 129.10, 128.55, 128.44, 97.13, 76.86, 76.32, 69.61, 66.70, 57.61, 35.44, 21.76, 18.21.

5.2.4. Methanolysis of epoxide 4 with 0.2N H_2SO_4 in anhydrous MeOH. A solution of the epoxide (0.50 mmol) in 0.2N H_2SO_4 in anhydrous MeOH (5 mL) was stirred at rt for 1 h. Dilution with saturated aqueous $NaHCO_3$, extraction with Et_2O and evaporation of the ether extracts afforded a crude liquid product which was analyzed by ^1H NMR (Table 2).

5.2.5. Aminolysis of epoxides 3–8 with $NHEt_2$–EtOH. *General procedure*. A solution of the epoxide (0.50 mmol) in anhydrous EtOH (4 mL) was treated with $NHEt_2$ (0.25 mL, 2.5 mmol) and the resulting reaction mixture was stirred at 80°C for the time shown in Tables 1 and 2. Evaporation of the organic solvent afforded a crude product which was filtered through a silica gel pad (a 7:2:1 hexane/AcOEt/NEt_3 mixture was used as the eluant) to give a crude product which was analyzed by ^1H NMR (Tables 1 and 2). In the case of epoxides **3** and **4**, the reaction mixture was diluted with ether and the organic solution washed (water) and evaporated.

The crude reaction product from epoxide **7** turned out to be constituted of practically pure *(−)-methyl 3-(N,N-diethylamino)-3,4,6-trideoxy-α-D-altropyranoside* (***C-3 product***) (0.107 g, 99% yield), as a liquid (Found: C, 60.54; H, 10.41; N, 6.76. $C_{11}H_{23}NO_3$ requires C, 60.80; H, 10.67; N, 6.45): $[\alpha]_D^{25}$=−35.0 (*c* 2.3, $CHCl_3$); ^1H NMR δ 4.50 (d, 1H, J=6.2 Hz), 4.21 (sextet, 1H, J=6.3 Hz), 3.48 (s, 3H), 3.39 (dd, 1H, J=11.0, 6.2 Hz), 2.88 (td, 1H, J=11.0, 6.2 Hz), 2.64 (dq, 2H, J=14.2, 7.1 Hz), 2.39 (dq, 2H, J=14.2, 7.1 Hz), 1.74 (ddd, 1H, J=12.9, 11.0, 6.2 Hz), 1.56 (dt, 1H, J=12.9, 6.2 Hz), 1.26 (d, 3H, J=6.3 Hz), 1.06 (t, 6H, J=7.1 Hz); ^{13}C NMR δ 103.40, 70.45, 66.83, 58.03, 56.37, 44.01, 28.28, 20.67, 15.04.

The crude reaction mixture of amino alcohols (0.087 g, 80% yield) from epoxide **8** was acetylated to give a corresponding mixture (0.090 g, 69% yield) of acetylated *C-2* and *C-3 product* (^1H NMR, Table 2) which were subjected to preparative TLC (an 8:2 hexane/acetone mixture was used as the eluant). Extraction of the faster moving band afforded pure *(+)-methyl 2-(N,N-diethylamino)-3-(O-acetyl)-2,4,6-trideoxy-α-D-altropyranoside* (***C-2 product***) (0.010 g, 8% yield), as a liquid (Found: C, 60.53; H, 10.07; N, 5.19. $C_{13}H_{25}NO_4$ requires C, 60.21; H, 9.72; N, 5.40): $[\alpha]_D^{25}$=+76.4 (*c* 1.3, $CHCl_3$); ^1H NMR δ 5.11 (q, 1H, J=6.0 Hz), 4.65 (d, 1H, J=2.7 Hz), 4.10 (sextet, 1H, J=6.0 Hz), 3.37 (s, 3H), 2.76 (dd, 1H, J=6.0, 2.7 Hz), 2.71 (dq, 2H, J=13.0, 7.2 Hz), 2.58 (dq, 2H, J=13.0, 7.2 Hz), 2.05 (s, 3H), 1.76 (t, 2H, J=6.0 Hz), 1.24 (d, 3H, J=6.0 Hz), 1.02 (t, 6H, J=7.2 Hz); ^{13}C NMR δ 171.07, 102.20, 67.64, 62.36, 62.13, 55.69, 45.17, 35.63, 22.11, 21.81, 14.95.

Extraction of the slower moving band afforded an 85:15 mixture of the corresponding free and acetylated *C-3 product* (0.058 g) which was dissolved in MeOH and treated with MeONa (0.010 g). After 24 h stirring at rt, evaporation of the solvent afforded a crude product which was filtered trough a short silica gel pad (ether was used as eluant) to give pure *(+)-methyl 3-(N,N-diethylamino)-3,4,6-trideoxy-α-D-glucopyranoside* (***C-3 product***) (0.045 g, 41% yield), as a liquid (Found: C, 61.08; H, 10.42; N, 6.11. $C_{11}H_{23}NO_3$ requires C, 60.80; H, 10.67; N, 6.45): $[\alpha]_D^{25}$=+158.7 (*c* 0.7, $CHCl_3$); ^1H NMR δ 4.90 (d, 1H, J=3.9 Hz), 3.91 (dqd, 1H, J=12.0, 6.0, 2.4 Hz), 3.52 (dd, 1H, J=10.7, 3.9 Hz), 3.44 (s, 3H), 3.07 (ddd, 1H, J=12.0, 10.7, 3.9 Hz), 2.64 (dq, 2H, J=13.0, 7.3 Hz), 2.39 (dq, 2H, J=13.0, 7.3 Hz), 1.73 (ddd, 2H, J=12.5, 3.9, 2.4 Hz), 1.30 (q, 1H, J=12.0 Hz), 1.19 (d, 3H, J=6.0 Hz), 1.05 (t, 6H, J=7.3 Hz); ^{13}C NMR δ 100.18, 68.88, 65.64, 57.96, 55.68, 43.84, 32.29, 21.98, 15.11.

The amino alcohols (^1H NMR) contained in the crude reaction mixture (0.086 g, 79% yield) from epoxide **6** turned out to be not separable by preparative TLC. The crude mixture was acetylated to give a mixture (0.084 g, 65% yield) of the corresponding acetates, not separable, as well.

C-2 product. ^1H NMR δ 4.76 (d, 1H, J=3.0 Hz), 3.29 (s, 3H), 2.79 (dq, 2H, J=14.2, 7.1 Hz), 2.03 (ddd, 1H, J=12.9, 4.9, 2.7 Hz), 1.76 (ddd, 1H, J=12.9, 9.5, 6.0 Hz), 1.30 (d, 3H, J=6.3 Hz), 0.96 (t, 6H, J=7.1 Hz). Acetate: ^1H NMR δ 5.27 (ddd, 1H, J=7.1, 5.3, 2.1 Hz), 4.61 (d, 1H, J=2.9 Hz), 4.05–3.88 (m, 1H), 3.34 (s, 3H), 2.85 (dd, 1H, J=7.3, 2.9 Hz), 1.99 (s, 3H), 1.22 (d, 3H, J=6.3 Hz), 0.93 (t, 6H, J=7.3 Hz).

C-3 product. ^1H NMR δ 4.13 (d, 1H, J=7.4 Hz), 3.50 (s, 3H), 3.13 (dd, 1H, J=10.1, 7.4 Hz), 2.29 (dq, 2H, J=13.3, 7.1 Hz), 1.63 (ddd, 1H, J=12.8, 3.9, 2.1 Hz), 1.20 (d, 3H, J=6.1 Hz), 0.98 (t, 6H, J=7.1 Hz). Acetate: ^1H NMR δ 4.70 (dd, 1H, J=10.5, 7.6 Hz), 4.18 (d, 1H, J=7.6 Hz), 3.41 (s, 3H), 2.26 (dq, 2H, J=13.3, 7.0 Hz), 1.99 (s, 3H), 1.20 (d, 3H, J=6.0 Hz), 0.89 (t, 6H, J=7.0 Hz).

The crude reaction product (0.091 g) from epoxide **5** was subjected to flash cromatography. Elution with a 5:5:0.2 CH_2Cl_2/hexane/NEt_3 mixture afforded pure *(−)-methyl 3-(N,N-diethylamino)-3,4,6-trideoxy-β-D-altropyranoside* (***C-3 product***) (0.072 g, 66% yield), as a liquid (Found: C, 60.49; H, 10.53; N, 6.75. $C_{11}H_{23}NO_3$ requires C, 60.80; H, 10.67; N, 6.45): $[\alpha]_D^{25}=-147.2$ (*c* 1.3, $CHCl_3$); ^{1}H NMR δ 4.80 (d, 1H, *J*=3.3 Hz), 4.09 (dqd, 1H, *J*=6.9, 5.4, 4.0 Hz), 3.53 (dd, 1H, *J*=9.5, 3.3 Hz), 3.42 (s, 3H), 3.13 (td, 1H, *J*=9.5, 4.0 Hz), 2.60 (dq, 2H, *J*=13.8, 6.8 Hz), 2.38 (dq, 2H, *J*=13.5, 6.8 Hz), 1.75 (ddd, 1H, *J*=13.3, 9.5, 5.4 Hz), 1.58 (dt, 1H, *J*=13.3, 4.0 Hz), 1.30 (d, 3H, *J*=6.9 Hz), 0.98 (t, 6H, *J*=6.8 Hz); ^{13}C NMR δ 101.36, 70.08, 68.84, 56.45, 54.37, 43.55, 29.68, 22.44, 14.35. Acetate, a liquid: ^{1}H NMR δ 4.96 (dd, 1H, *J*=5.1, 1.9 Hz), 4.74 (d, 1H, *J*=1.9 Hz), 3.92 (dqd, 1H, *J*=8.5, 6.4, 3.5 Hz), 3.41 (s, 3H), 2.89 (q, 1H, *J*=5.0 Hz), 2.61 (dq, 2H, *J*=14.0, 7.0 Hz), 2.53 (dq, 2H, *J*=13.9, 7.0 Hz), 2.05 (s, 3H), 1.70 (ddd, 1H, *J*=14.5, 5.0, 3.5 Hz), 1.56 (ddd, 1H, *J*=14.5, 8.5, 5.0 Hz), 1.22 (d, 3H, *J*=6.4 Hz), 0.91 (t, 6H, *J*=7.0 Hz); ^{13}C NMR δ 171.09, 99.21, 69.12, 68.37, 56.85, 55.87, 43.36, 31.76, 21.97, 21.73, 12.49.

The crude reaction product (0.142 g) from epoxide **3** was subjected to preparative TLC (an 85:15:5 hexane/AcOEt/NEt_3 mixture was used as the eluant). Extraction of the most intense band afforded pure *(+)-benzyl 3-(N,N-diethylamino)-2,3,6-trideoxy-α-D-gulopyranoside* (***C-3 product***) (0.110 g, 75% yield), as a liquid (Found: C, 69.75; H, 9.42; N, 4.86. $C_{17}H_{27}NO_3$ requires C, 69.59; H, 9.28; N, 4.77): $[\alpha]_D^{25}=+152.2$ (*c* 2.7, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 4.83 (dd, 1H, *J*=8.9, 3.6 Hz), 4.82 (d, 1H, *J*=11.8 Hz), 4.53 (d, 1H, *J*=11.8 Hz), 4.41 (dq, 1H, *J*=6.9, 5.6 Hz), 3.68 (dd, 1H, *J*=9.7, 5.6 Hz), 2.55–2.85 (m, 3H), 2.37 (dq, 2H, *J*=14.2, 7.1 Hz), 1.97 (dt, 1H, *J*=12.7, 3.6 Hz), 1.53 (dt, 1H, *J*=12.7, 8.9 Hz), 1.25 (d, 3H, *J*=6.9 Hz), 1.04 (t, 6H, *J*=7.1 Hz); ^{13}C NMR δ 138.34, 129.05, 128.70, 128.36, 96.13, 70.83, 70.47, 68.58, 58.11, 44.02, 29.74, 15.07, 13.46.

5.2.6. Aminolysis of epoxides 3–8 with $NHEt_2$–$LiClO_4$. *General procedure*. A solution of the epoxide (0.50 mmol) in anhydrous CH_3CN (4.0 mL) was treated with $NHEt_2$ (0.25 mL, 2.5 mmol) and anhydrous $LiClO_4$ (1.06 g, 10.0 mmol) and the reaction mixture was stirred at 80°C for the time shown in Tables 1 and 2. Dilution with ether and evaporation of the washed (water) ether extracts afforded a crude liquid product which was analyzed by ^{1}H NMR (Tables 1 and 2).

The crude product (0.145 g) from epoxide **4** was subjected to preparative TLC (a 9:1 hexane/NEt_3 mixture was used as the eluant). Extraction of the two most intense bands afforded the corresponding *C-3* (0.065 g, 44% yield) and *C-4 product* (0.053 g, 36% yield).

(+)-Benzyl 4-(N,N-diethylamino)-2,4,6-trideoxy-α-D-gulopyranoside (***C-4 product***), a liquid (Found: C, 69.32; H, 9.14; N, 4.53. $C_{17}H_{27}NO_3$ requires C, 69.59; H, 9.28; N, 4.77): $[\alpha]_D^{25}=+70.2$ (*c* 0.8, $CHCl_3$); ^{1}H NMR δ 7.18–7.40 (m, 5H), 4.98 (t, 1H, *J*=3.6 Hz), 4.73 (d, 1H, *J*=11.9 Hz), 4.50 (d, 1H, *J*=11.9 Hz), 4.41 (dq, 1H, *J*=6.7, 4.5 Hz), 3.90–4.02 (m, 1H), 2.81 (dq, 2H, *J*=13.8, 7.0 Hz), 2.49–2.75 (m, 3H), 2.13 (dt, 1H, *J*=14.2, 3.6 Hz), 1.91 (dt, 1H, *J*=14.2, 3.6 Hz), 1.26 (d, 3H, *J*=6.7 Hz), 1.03 (t, 6H, *J*=7.0 Hz); ^{13}C NMR δ 138.08, 129.13, 128.58, 128.49, 97.16, 70.00, 65.05, 64.12, 62.89, 45.68, 35.49, 18.01, 15.69.

(+)-Benzyl 3-(N,N-diethylamino)-2,3,6-trideoxy-α-D-glucopyranoside (***C-3 product***), a semisolid (Found: C, 69.19; H, 9.02; N, 4.39. $C_{17}H_{27}NO_3$ requires C, 69.59; H, 9.28; N, 4.77): $[\alpha]_D^{25}=+42.9$ (*c* 0.7, $CHCl_3$); ^{1}H NMR δ 7.20–7.40 (m, 5H), 4.99 (unresolved dd, 1H, *J*=2.8 Hz), 4.71 (d, 1H, *J*=12.1 Hz), 4.46 (d, 1H, *J*=12.1 Hz), 3.99 (dq, 2H, *J*=14.2, 7.1 Hz), 3.76 (dq, 1H, *J*=8.4, 6.2 Hz), 2.98–3.17 (m, 2H), 2.34 (dq, 2H, *J*=14.2, 7.1 Hz), 1.80–1.96 (m, 1H), 1.55–1.74 (m, 1H), 1.31 (d, 3H, *J*=6.2 Hz), 1.05 (t, 6H, *J*=7.1 Hz); ^{13}C NMR δ 138.66, 129.01, 128.40, 128.21, 97.47, 72.09, 70.01, 69.22, 58.84, 43.75, 28.75, 19.10, 15.27.

5.2.7. Reaction of epoxides 3–8 with PhSH–NEt_3. *General procedure*. A solution of the epoxide (0.50 mmol) in MeOH (0.5 mL) was treated with PhSH (0.153 mL, 1.50 mmol) and NEt_3 (0.26 mL, 2.0 mmol) and the resulting reaction mixture was stirred at rt for the time shown in Tables 1 and 2. Evaporation of the solvent afforded a crude product which was analyzed by ^{1}H NMR (Tables 1 and 2).

The crude reaction mixture (0.165 g) from epoxide **3** was subjected to preparative TLC (a 7:3 hexane/AcOEt mixture was used as the eluant). Extraction of the two most intense bands afforded the corresponding C-3 (0.128 g, 78% yield) and *C-4 product* (0.008 g, 5% yield).

(+)-Benzyl 4-(thiophenyl)-2,4,6-trideoxy-α-D-glucopyranoside (***C-4 product***), a solid, mp 72–73°C (recrystallized from hexane) (Found: C, 69.21; H, 6.44. $C_{19}H_{22}O_3S$ requires C, 69.06; H, 6.71): $[\alpha]_D^{25}=+70.8$ (*c* 0.5, $CHCl_3$); ^{1}H NMR δ 7.41–7.55 (m, 2H), 7.15–7.40 (m, 8H), 5.00 (dd, 1H, *J*=3.5, 1.3 Hz), 4.62 (d, 1H, *J*=12.0 Hz), 4.40 (d, 1H, *J*=12.0 Hz), 3.95 (dt, 1H, *J*=10.8, 5.0 Hz), 3.80 (dq, 1H, *J*=10.6, 6.2 Hz), 2.63 (t, 1H, *J*=10.5 Hz), 2.29 (ddd, 1H, *J*=13.0, 4.9, 1.3 Hz), 1.76 (ddd, 1H, *J*=12.9, 11.3, 3.5 Hz), 1.37 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 138.42, 133.92, 133.40, 129.83, 129.06, 128.55, 128.27, 97.24, 69.47, 68.51, 66.15, 61.78, 38.53, 20.09 (1×Ph signals unresolved).

(+)-Benzyl 3-(thiophenyl)-2,3,6-trideoxy-α-D-gulopyranoside (***C-3 product***), a liquid (Found: C, 68.81; H, 6.35. $C_{19}H_{22}O_3S$ requires C, 69.06; H, 6.71): $[\alpha]_D^{25}=+52.0$ (*c* 1.6, $CHCl_3$); ^{1}H NMR δ 7.10–7.50 (m, 10H), 4.89 (dd, 1H, *J*=3.7, 1.3 Hz), 4.79 (d, 1H, *J*=12.4 Hz), 4.52 (d, 1H, *J*=12.4 Hz), 4.55 (q, 1H, *J*=6.8 Hz), 3.40–3.55 (m, 2H), 2.45 (ddd, 1H, *J*=14.9, 5.5, 4.2 Hz), 1.95 (ddd, 1H, *J*=14.9, 3.5, 1.7 Hz), 1.17 (d, 3H, *J*=6.8 Hz); ^{13}C NMR δ 138.52, 136.90, 131.11, 129.69, 128.96, 128.11, 127.38, 96.24, 70.58, 69.64, 63.12, 45.88, 30.30, 17.19 (1×Ph signals unresolved).

The crude reaction mixture (0.125 g) from epoxide **8** was subjected to preparative TLC (an 85:15 hexane/AcOEt mixture was used as the eluant). Extraction of the most

intense bands afforded the corresponding C-2 (0.035 g, 28% yield) and *C-3 product* (0.076 g, 60% yield).

(+)-Methyl 2-(thiophenyl)-2,4,6-trideoxy-α-D-altropyranoside (***C-2 product***), a liquid (Found: C, 61.28; H, 7.32. $C_{13}H_{18}O_3S$ requires C, 61.39; H, 7.13): $[\alpha]_D^{25}=+6.0$ (*c* 1.9, $CHCl_3$); ^{1}H NMR δ 7.10–7.41 (br s, 5H), 4.79 (m, 1H), 3.91–4.18 (m, 2H), 3.24–3.40 (m, 1H), 3.32 (s, 3H), 1.93 (ddd, 1H, *J*=14.1, 11.6, 2.7 Hz), 1.56–1.71 (m, 1H), 1.19 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 135.18, 131.60, 129.87, 127.87, 102.23, 68.64, 60.36, 56.06, 50.05, 36.07, 21.81.

(+)-Methyl 3-(thiophenyl)-3,4,6-trideoxy-α-D-glucopyranoside (***C-3 product***), a liquid (Found: C, 61.23; H, 7.01. $C_{13}H_{18}O_3S$ requires C, 61.39; H, 7.13): $[\alpha]_D^{25}=+171.5$ (*c* 0.8, $CHCl_3$); ^{1}H NMR δ 7.42–7.58 (m, 2H), 7.20–7.42 (m, 3H), 4.75 (d, 1H, *J*=3.3 Hz), 3.87 (dqd, 1H, *J*=11.7, 6.2, 2.2 Hz), 3.33–3.56 (m, 1H), 3.43 (s, 3H), 3.31 (dt, *J*=11.7, 3.9 Hz), 1.97 (ddd, 1H, *J*=13.5, 3.9, 2.2 Hz), 1.38 (dt, 1H, *J*=13.5, 11.7 Hz), 1.12 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 134.97, 132.61, 129.61, 128.64, 100.02, 71.70, 65.38, 55.75, 48.30, 40.50, 21.31. Acetate, a liquid: $[\alpha]_D^{25}=+91.9$ (*c* 1.8, $CHCl_3$); ^{1}H NMR δ 7.47–7.52 (m, 2H), 7.17–7.47 (m, 3H), 4.83 (dd, 1H, *J*=11.0, 3.5 Hz), 4.76 (d, 1H, *J*=3.5), 3.92 (dqd, 1H, *J*=12.4, 6.2, 4.2 Hz), 3.61 (ddd, 1H, *J*=12.4, 11.0, 4.2 Hz), 3.38 (s, 3H), 2.05 (ddd, 1H, *J*=13.5, 4.2, 2.2 Hz), 1.98 (s, 3H), 1.46 (dt, 1H, *J*=13.2, 12.4 Hz), 1.15 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 171.15, 133.84, 129.56, 128.18, 97.92, 74.09, 64.94, 55.60, 44.04, 40.47, 21.50, 21.26 (1×Ph signal unresolved).

The crude reaction product (0.127 g) from epoxide **7** was subjected to flash cromatography. Elution with a 7:3 hexane/AcOEt mixture afforded pure *(−)-methyl 3-(thiophenyl)-3,4,6-trideoxy-α-D-altropyranoside* (***C-3 product***) (0.119 g, 94% yield), as a liquid (Found: C, 61.44; H, 7.21. $C_{13}H_{18}O_3S$ requires C, 61.39; H, 7.13): $[\alpha]_D^{25}=-2.0$ (*c* 2.9, $CHCl_3$); ^{1}H NMR δ 7.36–7.48 (m, 2H), 7.17–7.36 (m, 3H), 4.60 (d, 1H, *J*=3.3 Hz), 4.23 (dqd, 1H, *J*=8.7, 6.3, 3.6 Hz), 3.69 (dd, 1H, *J*=5.3, 3.3 Hz), 3.44 (s, 3H), 3.38 (q, 1H, *J*=5.3 Hz), 1.95 (ddd, 1H, *J*=14.0, 8.7, 5.3 Hz), 1.73 (ddd, 1H, *J*=14.0, 5.3, 3.6 Hz), 1.24 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 135.51, 132.40, 129.65, 127.78, 101.86, 70.48, 63.43, 56.13, 46.89, 34.56, 20.84.

The thioethers present in the crude reaction mixture (0.127 g) from epoxide **6** turned out to be not separable by preparative TLC. Acetylation afforded a crude reaction mixture (0.142 g, 96% yield), which was subjected to preparative TLC (CH_2Cl_2 was used as the eluant). Extraction of the two most intense bands afforded the corresponding pure acetylated *C-2* (0.025 g, 17% yield) and *C-3 product* (0.054 g, 36% yield).

(−)-Methyl 2-(thiophenyl)-3-(O-acetyl)-2,4,6-trideoxy-β-D-altropyranoside (***C-2 product***), a solid, mp 70.5–71.5°C (recrystallized from hexane) (Found: C, 61.03; H, 6.52. $C_{15}H_{20}O_4S$ requires C, 60.79; H, 6.80): $[\alpha]_D^{25}=-66.6$ (*c* 1.2, $CHCl_3$); ^{1}H NMR δ 7.31–7.50 (m, 2H), 7.09–7.31 (m, 3H), 5.13 (q, 1H, *J*=3.2 Hz), 4.76 (d, 1H, *J*=2.1 Hz), 3.87 (dqd, 1H, *J*=11.1, 6.3, 2.4 Hz), 3.50 (s, 3H), 3.33–3.43 (m, 1H), 1.99 (s, 3H), 1.89–2.03 (m, 1H), 1.50–1.64 (m, 1H), 1.22 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 170.48, 135.66, 131.72, 129.59, 127.46, 100.36, 72.65, 68.74, 57.28, 51.37, 33.42, 21.73, 21.85.

(−)-Methyl 3-(thiophenyl)-2-(O-acetyl)-3,4,6-trideoxy-β-D-glucopyranoside (***C-3 product***), a liquid (Found: C, 60.46; H, 6.69. $C_{15}H_{20}O_4S$ requires C, 60.79; H, 6.80): $[\alpha]_D^{25}=-3.0$ (*c* 2.1, $CHCl_3$); ^{1}H NMR δ 7.31–7.51 (m, 2H), 7.11–7.31 (m, 3H), 4.73 (dd, *J*=10.7, 7.7 Hz), 4.19 (d, 1H, *J*=7.7 Hz), 3.54 (dqd, 1H, *J*=11.0, 6.2, 1.9 Hz), 3.38 (s, 3H), 3.12 (ddd, 1H, *J*=13.0, 10.7, 4.4 Hz), 1.93 (ddd, 1H, *J*=13.0, 4.4, 1.9 Hz), 1.88 (s, 3H), 1.34 (td, 1H, *J*=13.0, 11.0 Hz), 1.14 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 170.57, 134.45, 133.16, 129.58, 128.50, 103.62, 73.77, 71.09, 57.05, 48.15, 40.11, 21.50, 21.30.

The crude reaction product (0.126 g) from epoxide **5** was subjected to flash cromatography. Elution with a 6:4 hexane/Et_2O mixture afforded pure *(−)-methyl 3-(thiophenyl)-3,4,6-trideoxy-β-D-altropyranoside* (***C-3 product***) (0.093 g, 73% yield), as a liquid (Found: C, 61.43; H, 7.22. $C_{13}H_{18}O_3S$ requires C, 61.39; H, 7.13): $[\alpha]_D^{25}=-28.4$ (*c* 2.1, $CHCl_3$); ^{1}H NMR δ 7.10–7.41 (m, 5H), 4.73 (d, 1H, *J*=0.7 Hz), 3.87 (dqd, 1H, *J*=10.6, 6.3, 2.4 Hz), 3.53–3.66 (m, 2H), 3.45 (s, 3H), 1.99 (ddd, 1H, *J*=14.5, 10.6, 4.0 Hz), 1.58 (dt, 1H, *J*=14.1, 2.4 Hz), 1.78 (d, 3H, *J*=6.3 Hz); ^{13}C NMR δ 134.78, 131.66, 129.81, 127.73, 99.60, 68.56, 56.89, 46.93, 33.30, 21.78 (1×*C*H signals unresolved). Acetate, a liquid: $[\alpha]_D^{25}=-67.1$ (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 7.38 (dd, 2H, *J*=8.2, 1.4 Hz), 7.10–7.21 (m, 3H), 4.89 (dd, 1H, *J*=3.2, 1.3 Hz), 4.85 (d, 1H, *J*=1.3 Hz), 3.92 (dqd, 1H, *J*=10.6, 6.2, 2.3 Hz), 3.55–3.65 (m, 1H), 3.45 (s, 3H), 2.04 (s, 3H), 1.92 (ddd, 1H, *J*=14.2, 10.6, 4.7 Hz), 1.65 (dt, 1H, *J*=14.2, 2.3 Hz), 1.22 (d, 3H, *J*=6.2 Hz); ^{13}C NMR δ 171.00, 134.50, 131.33, 129.82, 127.80, 98.66, 69.76, 68.60, 57.34, 45.24, 34.12, 21.73 (1×Me signals unresolved).

5.2.8. Reaction of epoxides 3–8 with PhSH–$LiClO_4$. *General procedure*. A solution of the epoxide (0.50 mmol) in anhydrous MeCN (1.0 mL) containing PhSH (0.077 mL, 0.75 mmol) and anhydrous $LiClO_4$ (0.266 g, 2.5 mmol) was stirred at 80°C for the time shown in Tables 1 and 2. Dilution with ether and evaporation of the washed (water) ether extracts afforded a crude liquid product which was analyzed by ^{1}H NMR (Tables 1 and 2). In the case of epoxides **5**–**8**, the solvent (MeCN) was evaporated and the crude reaction product was filtered through a silica gel pad (a 7:3 hexane/AcOEt mixture was used as the eluant).

The crude reaction mixture (0.165 g) from epoxide **4** was subjected to preparative TLC (CH_2Cl_2 was used as the eluant). Extraction of the two most intense bands afforded the corresponding *C-3* (0.059 g, 36% yield) and *C-4 product* (0.073 g, 44% yield).

(+)-Benzyl 4-(thiophenyl)-2,4,6-trideoxy-α-D-gulopyranoside (***C-4 product***), a liquid (Found: C, 69.18; H, 6.48. $C_{19}H_{22}O_3S$ requires C, 69.06; H, 6.71): $[\alpha]_D^{25}=+100.5$ (*c* 1.2, $CHCl_3$); ^{1}H NMR δ 7.15–7.45 (m, 10H), 5.04 (dd, 1H, *J*=3.6, 1.2 Hz), 4.72 (d, 1H, *J*=11.8 Hz), 4.52 (d, 1H, *J*=11.8 Hz), 4.63 (dq, 1H, *J*=6.5, 2.2 Hz), 4.09 (dq, 1H, *J*=9.3, 2.6 Hz), 3.20–3.29 (m, 1H), 2.46 (dt, 1H, *J*=14.7, 3.6 Hz), 1.85 (ddd, *J*=14.7, 2.6, 1.2 Hz), 1.40 (d, 3H,

J=6.5 Hz); ^{13}C NMR δ 137.65, 136.11, 131.46, 129.74, 129.19, 128.67, 127.35, 98.12, 70.29, 68.87, 61.58, 55.42, 30.97, 19.68 (1×Ph signals unresolved).

(+)-Benzyl 3-(thiophenyl)-2,3,6-trideoxy-α-D-glucopyranoside (***C-3 product***), a liquid (Found: C, 68.90; H, 6.55. $C_{19}H_{22}O_3S$ requires C, 69.06; H, 6.71): $[\alpha]_D^{25}$=+94.6 (*c* 1.3, $CHCl_3$); ^{1}H NMR δ 7.40–7.53 (m, 2H), 7.21–7.40 (m, 8H), 4.81 (unresolved dd, 1H, J=3.1 Hz), 4.67 (d, 1H, J=11.9 Hz), 4.44 (d, 1H, J=11.9 Hz), 3.81 (dq, 1H, J=9.0, 6.1 Hz), 3.37 (ddd, 1H, J=13.0, 10.2, 3.8 Hz), 3.04 (ddd, 1H, J=10.2, 9.0, 1.1 Hz), 2.19 (ddd, 1H, J=13.0, 3.8, 0.9 Hz), 1.73 (td, 1H, J=13.0, 3.8 Hz), 1.29 (d, 3H, J=6.1 Hz); ^{13}C NMR δ 138.32, 135.22, 131.42, 129.71, 129.07, 128.96, 128.53, 128.38, 96.53, 74.54, 69.56, 69.36, 48.94, 37.55, 19.02.

Acknowledgements

This work was supported by the Universitá di Pisa and the Ministero della Universitá e della Ricerca Scientifica e Tecnologica (MURST), Roma. P. C. gratefully acknowledges Merck Research Laboratories for the generous financial support from 2001 ADP Chemistry Award.

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4. Standard reaction conditions: oxirane ring opening reactions carried out with a nucleophile under proton acid catalysis (NaN_3/NH_4Cl in MeOH–H_2O, MeOH/H_2SO_4) or in the presence of the nucleophile in an appropriate polar solvent (MeONa in MeOH, NaN_3 in DMF, $NHEt_2$ in EtOH, PhSH in MeOH–NEt_3). Chelating reaction conditions: oxirane ring opening reactions carried out with a nucleophile in the presence of a metal salt in a polar aprotic solvent (MeOH/$LiClO_4$, NaN_3/$LiClO_4$ in MeCN, $NHEt_2$/$LiClO_4$ in MeCN, PhSH/$LiClO_4$ in MeCN).
5. The *cis*/*trans* descriptors preceding the number for each epoxide indicate the relative configuration between the oxirane ring and methyl group (first descriptor) and the OR group (R=Me or benzyl) (second descriptor), respectively.
6. The indifferent use of benzyl or methyl glycosides as derivatives of epoxides **3**–**8** is dictated by the consideration that the nature of the acetal group should not reasonably influence the stereo- and regiochemical behavior of these epoxides.
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10. Unlike from previously reported results,[9c] the dehalogenation of (+)-**30α** by means of the Bu_3SnH/AIBN protocol led to an almost 1:1 mixture of diol (+)-**31α** and chloro diol **32**,[9e] which turned out to be difficult to separate.
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13. In search of a stereoselective synthesis of epoxide (+)-**7**, the diacetoxy derivative (+)-**39**α was checked in mono-deprotection procedures in order to get the monoacetate **40**α, regioselectively. Unfortunately, the best result obtained (lipase PPL, phosphate buffer, pH 7) afforded a mixture of monoacetates **34**α and **40**α showing a regioselectivity (60%) towards the monoacetate **40**α, necessary for the synthesis of epoxide (+)-**7**, lower than the corresponding regioselectivity (85%) towards monotosylate **37**, found in the monotosylation of diol (+)-**31**α, which leads to epoxide (+)-**7**, as well.
14. Unfortunately, we were not able to obtain the more satisfactory results, recently described.[15a] As a consequence, our present results confirm, in accordance with Jones result, the decidedly different chemical behavior of anomers (−)-**29**β and (+)-**29**α in the reaction with SO_2Cl_2,[15b] and show the non-applicability of this procedure to an effective synthesis of diol (−)-**31**β and, consequently of epoxides (−)-**5** and (−)-**6** (Scheme 5).
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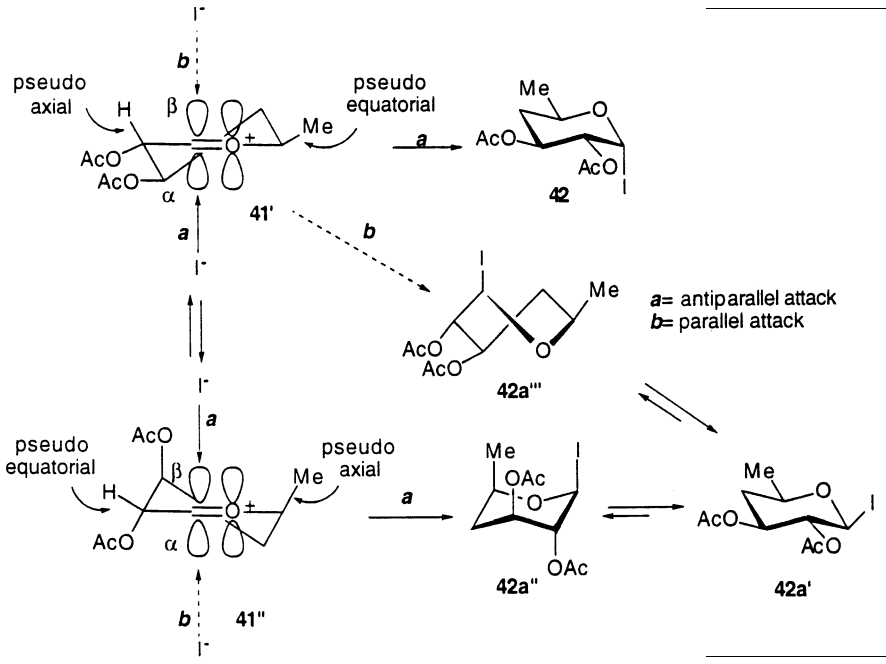
18. Admitting that an antiparallel (axial) attack of the nucleophile (I^-) on oxonium ion **41**, leading to the axial iodide **42** through a chair-like transition state (route ***a*** from conformer **41′** in the following scheme) should be preferred with respect to the corresponding parallel (equatorial) attack, leading to the equatorial iodide **42a** through a twist-like transition state (route ***b*** from **41′**), the diastereoisomeric equatorial iodide **42a** could be reasonably obtained only by an attack of I^- on the β face of the intermediate oxonium ion **41**, reacting through its conformer **41″** (route ***a***). However, as tentatively shown in the following scheme, this attack turns out to be particularly unfavored because suffering from an 1,3-*syn* diaxial interaction with the methyl and the AcO groups in C(5) and C(3), respectively. See: (a) Sayer, J. M.; Yagi, H.;

Silverton, J. V.; Friedman, S. L.; Whalen, D. L.; Jerina, D. M. *J. Am. Chem. Soc.* **1982**, *104*, 1972–1978 and references therein. For related considerations in the cyclohexane system see: (b) Eliel, E. L.; Allinger, N. J.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Wiley: New York, 1965; pp 307–314. (c) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 729–730.



19. Szarek, W. A.; Zamojski, A.; Gibson, A. R.; Vyas, D. M.; Jones, J. K. N. *Can. J. Chem.* **1976**, *54*, 3783–3793.
20. Note the completely different regioselectivity observed with anomeric diols (+)-**31**α and (−)-**31**β when subjected to monoacetylation in the presence of lipase PS: selective protection of the C(2)–OH in the case of (+)-**31**α and of the C(3)–OH in the case of (−)-**31**β. Evidently, the axial (in **31**α) or equatorial direction (in **31**β) of the acetal –OMe group plays an important role in favoring or disfavoring the reactivity of the equatorial C(2)–OH group, respectively.
21. Epoxides **5** and **6** have been previously described as a racemic mixture: Berube, G.; Luce, E.; Jankowski, K. *Bull. Soc. Chim. Fr.* **1983**, 109–111.
22. In the α-series, the C(3)–OH selectivity observed under Mitsunobu operating conditions led to the epoxide (+)-**8**, also obtained through the long monoacetylation–mesylation–saponification–cyclization procedure starting from diol (+)-**31**α. On the contrary, in the β-series, as a result of the opposite selectivity obtained in the lipase PS-catalyzed monoacetylation of diol (−)-**31**β, the Mitsunobu protocol leads to epoxide (−)-**6**, the diastereoisomer of epoxide (−)-**5** obtained through the alternative long sequence.
23. Alcohol (±)-**47** was prepared by an hetero Diels–Alder cycloaddition between Danishefsky diene (**45**) and acetaldehyde. The obtained dihydropyranone (±)-**46** is reduced by DIBAL to the desired alcohol (±)-**47** (Scheme 6). See: Danishefsky, S.; Kerwin, Jr., J. F. *J. Org. Chem.* **1982**, *47*, 1597–1598 and references therein.
24. The absence in the reaction mixture of products possessing an inverted configuration at C(2) (a *manno* configuration) reasonably rules out the formation of the diastereoisomeric β-epoxide in the oxidation of glycal (±)-**48**, in agreement with the sensitiveness of the DMDO to steric effects. Accordingly, the attack of the DMDO occurs on the less hindered α-face, opposite the β-direction of the substituents present in C(3) and C(5), to give α-epoxide (±)-**49**α, as observed.
25. (a) Crotti, P.; Di Bussolo, V.; Favero, L.; Macchia, F.; Pineschi, M. *Gazz. Chim. Ital.* **1997**, *127*, 273–275. (b) Schaus, S. E.; Bránalt, J.; Jacobsen, E. N. *J. Org. Chem.* **1998**, *63*, 403–405.
26. Examination of the ^{1}H NMR spectra of epoxides **1**–**8**, and in particular the values of the coupling constant of the anomeric proton in **1** and **2** (J=8.6–9.1 Hz)[2] and **3** and **4** (J=4.7–5.0 Hz), as previously observed in the corresponding methyl glycosides,[3] and of the decoupled proton α to the methyl group in **5**–**8** (J=10.8–11.2 Hz), clearly indicates for these protons a preferred equatorial (in **3** and **4**) and an axial orientation (in **1**, **2** and **5**–**8**), respectively, and, consequently, a clear preference of epoxides **1**–**8** for the corresponding conformer a with the methyl group equatorial (Schemes 8 and 9).[2,3]
27. Also in the few cases in which the opening reactions under standard conditions are not completely C-3 stereoselective, the corresponding results under chelating conditions show an increase or the only presence of *C-3 products*, in accordance with the rationalization given.
28. These results would indicate that no chelation can occur between the oxirane oxygen and the acetalic OR group, if this makes the epoxide adopt an all axial conformer such as **1b** (from **1**) and **5b** (from **5**).[2]
29. Actually, it is not clear why epoxide **6** is not sensitive, to some extent, to different operating conditions as diastereoisomeric epoxide **8** is.
30. In accordance with the rationalization given, the results with a medium strength nucleophile such as $NHEt_2$ determine only a slight increase of C-2 regioselectivity (Table 2, entries 33 and 34).