Regiochemical Control of the Ring-Opening of Epoxides by Means of Chelating Processes, 13[◇]

Synthesis and Ring-Opening Reactions of the Diastereoisomeric *cis*- and *trans*-Epoxides Derived from 3-(Benzyloxy)cyclopentene and 2-(Benzyloxy)-2,5-dihydrofuran

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

Dipartimento di Chimica Bioorganica, Universita` di Pisa,
Via Bonanno 33, I-56126 Pisa, Italy
E-mail: crotti@farm.unipi.it

Received April 17, 1998

Keywords: Epoxides / Regioselectivity / Nucleophilic additions / Synthetic methods

The regiochemical outcome of the ring-opening of epoxides bearing remote polar functionalities has been established in the case of carbocyclic (**1** and **2**) and the corresponding furanosidic (**3** and **4**) title epoxides. Under standard conditions, the regioisomeric *C-1 products* are the sole (from *trans* epoxides **2** and **4**) or predominant (from *cis* epoxides **1** and **3**) ring-opening products. However, under chelating conditions, and only in the case of the *cis* epoxides **1** and **3**, a consistent increase in C-2 selectivity is unexpectedly observed.

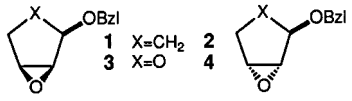
Introduction

Recently developed effective procedures for obtaining chiral epoxides with outstanding enantiomeric excesses[1] have greatly extended the use of these heterocycles for the simultaneous construction of two adjacent stereodefined chiral centres, as a consequence of their ability to react with a large variety of nucleophiles in a completely *anti* stereoselective fashion.[2] However, in many cases, the regiochemistry of this reaction is unfortunately random, thus detracting from the excellent stereochemical results. For this reason, extensive studies on aliphatic and cycloaliphatic oxirane systems have been carried out aimed at finding procedures that offer improved regiochemical control in nucleophilic ring-opening reactions. In this respect, the use of an *O*-heterofunctionality (an ether or acetal group) in an allylic or homoallylic relationship to the oxirane ring has been found to give satisfactory results.[3]

As an extension of previous studies on the regiochemical behavior of epoxides derived from five-membered cyclic systems,[4] we have now synthesized and studied the carbocyclic epoxides *cis* **1** and *trans* **2**, as well as the corresponding furanosidic derivatives *cis* **3** and *trans* **4**. In each of the epoxides **1**−**4**, the *O*-heterofunctionality [ether functionality (OBzl) in **1** and **2**, or an acetal in **3** and **4**] is in an allylic relationship to the oxirane ring.

Results

The *m*-CPBA oxidation of the unsaturated alcohol **5**, obtained by DIBAL-H reduction of 2-cyclopenten-1-one,[5] afforded a 98:2 mixture of epoxy alcohols *cis* **6** and *trans* **7**,[6] which was directly alkylated using the BnBr/NaH protocol to give a corresponding mixture of the benzylated epoxides *cis* **1** and *trans* **2**.[6a] Simple filtration through a silica gel column yielded pure *cis* epoxide **1**. When *m*-CPBA oxidation was performed on the benzylated olefin **8**, the obtained 34:66 mixture of epoxides *cis* **1** and *trans* **2** could be separated by flash chromatography. A similar stereochemical result (epoxide *cis* **1**/epoxide *trans* **2** = 25:75) was also obtained upon base-catalyzed cyclization of the 67:33 mixture of bromohydrins **9** and **10** obtained from the reaction of olefin **8** with NBS in aqueous THF. Bromohydrins **9** and **10** were the only addition products of this reaction, the regioisomeric *trans* **11** and **12** being completely absent in the crude product mixture. In fact, **11** and **12** could only be obtained by reaction of epoxides **1** and **2**, respectively, with HBr in $CHCl_3$ (Scheme 1 and Tables 1 and 2).[7]



The approximately 2:1 ratio of the stereoisomeric bromohydrins **9** and **10** generated in the reaction of **8** with NBS in THF/H_2O can be expected to reflect a similar selectivity in the formation of the corresponding bromonium ions **15** and **16**, which results from a favorable interaction between the electrophile and the *O*-heterofunctionality, as illustrated in structure **13** (Scheme 2). Bromonium ions **15** and **16** are then attacked by the nucleophile (H_2O) in a completely regioselective manner at C(1) to give bromohydrins **9** and **10**, respectively (Scheme 2).

Epoxides **3** and **4** were prepared as shown in Scheme 3. The reaction of 2,3-dihydrofuran with PhSeCl in the pres-

[◇] For part XII, see ref.[3a].

  1434−193X/98/0808−1675 $ 17.50+.50/0

Scheme 1

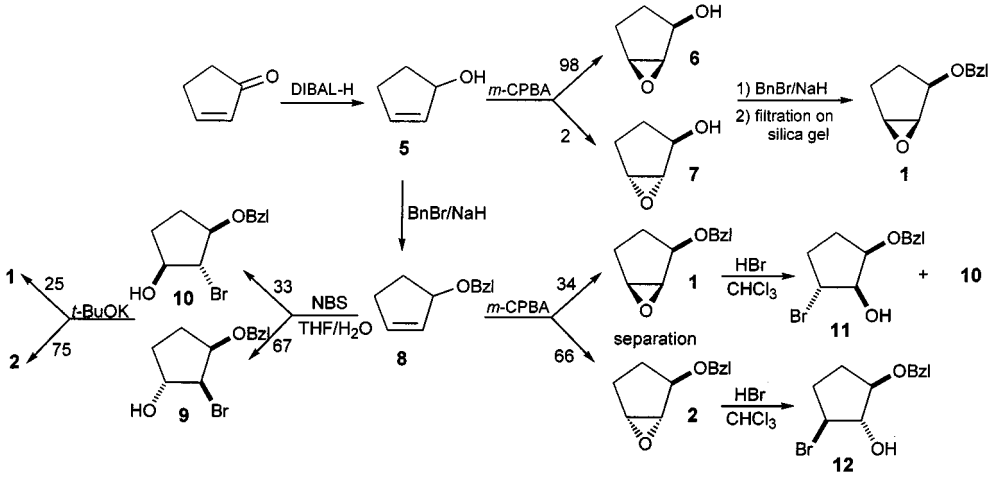


Table 1. Regioselectivity of the ring-opening reactions of the *cis* epoxides **1** and **3** under standard and chelating conditions

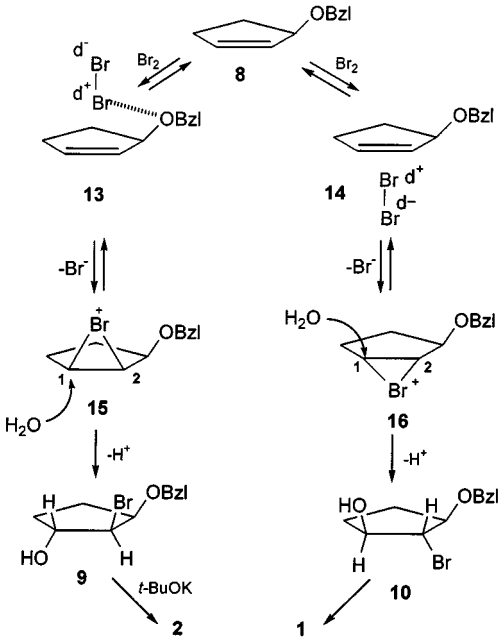
entry	epoxide	reagents	solvent	reaction time and temperature	*C-1 product*		*C-2 product*		yield (%)
1	**1**	HBr	$CHCl_3$	10 min (r.t.)	**11**	86	**10**	14	94
2	**1**	$MeOH/H_2SO_4$	MeOH	30 min (r.t.)	**21**	93	**22**	7	96
3	**1**	$MeOH/LiClO_4$ 10 M	MeOH	24 h (80°C)		95		5	88
4	**1**	NaN_3/NH_4Cl	$MeOH/H_2O$	18 h (80°C)	**23**	93	**24**	7	95
5	**1**	$NaN_3/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		89		11	89
6	**1**	$NHEt_2$	EtOH	3 days (80°C)	**25**	87	**26**	13	94
7	**1**	$NHEt_2/LiClO_4$ 5 M	MeCN	18 h (80°C)		70		30	90
8	**1**	$PhSH/NEt_3$	MeOH	18 h (r.t.)	**27**	80	**28**	20	95
9	**1**	$PhSH/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		62		38	93
10	**1**	$LiAlH_4$	pentane	2 h (r.t.)	**29**	55	**30**	45	97
11	**1**	$LiAlH_4$/crown	pentane	18 h (r.t.)		70		30	40[a]
12	**3**	NaN_3/NH_4Cl	$MeOH/H_2O$	60 h (80°C)	**31**	84	**32**	16	96
13	**3**	$NaN_3/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		73		27	92
14	**3**	$NHEt_2$	EtOH	3 days (80°C)	**33**	85	**34**	15	94
15	**3**	$NHEt_2/LiClO_4$ 5 M	MeCN	18 h (80°C)		71		29	89
16	**3**	$PhSH/NEt_3$	MeOH	18 h (r.t.)	**35**	80	**36**	20	96
17	**3**	$PhSH/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		42		58	90
18	**3**	$LiAlH_4$	pentane	2 h (r.t.)	**37**	35	**38**	65	95
19	**3**	$LiAlH_4$/crown	pentane	18 h (r.t.)		84		16	50[b]

[a] 60% of starting epoxide was still present. – [b] 50% starting epoxide was still present.

Table 2. Regioselectivity of the ring-opening reactions of the *trans* epoxides **2** and **4** under standard and chelating conditions

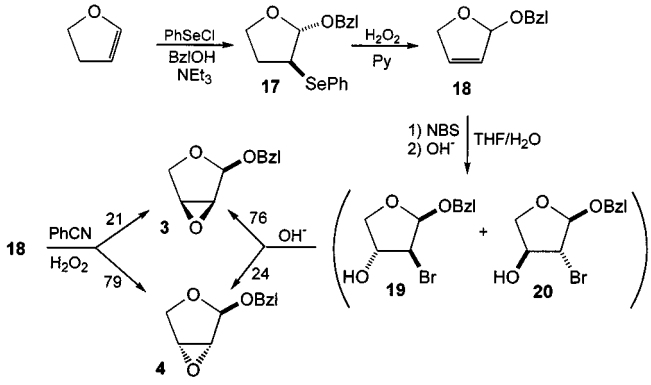
entry	epoxide	reagents	solvent	reaction time and temperature	*C-1 product*		*C-2 product*		yield (%)
1	**2**	HBr	$CHCl_3$	10 min (r.t.)	**12**	>99	**9**	<1	90
2	**2**	$MeOH/H_2SO_4$	MeOH	30 min (r.t.)	**39**	>99	**48**	<1	94
3	**2**	$MeOH/LiClO_4$ 10 M	MeOH	24 h (80°C)		>99		<1	85
4	**2**	NaN_3/NH_4Cl	$MeOH/H_2O$	18 h (80°C)	**40**	>99	**49**	<1	91
5	**2**	$NaN_3/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		>99		<1	89
6	**2**	$NHEt_2$	EtOH	3 days (80°C)	**41**	>99	**50**	<1	88
7	**2**	$NHEt_2/LiClO_4$ 5 M	MeCN	18 h (80°C)		>99		<1	85
8	**2**	$PhSH/NEt_3$	MeOH	18 h (r.t.)	**42**	>99	**51**	<1	92
9	**2**	$PhSH/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		>99		<1	91
10	**2**	$LiAlH_4$	pentane	2 h (r.t.)	**43**	>99	**52**	<1	96
11	**4**	NaN_3/NH_4Cl	$MeOH/H_2O$	60 h (80°C)	**44**	>99	**53**	<1	94
12	**4**	$NaN_3/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		>99		<1	89
13	**4**	$NHEt_2$	EtOH	3 days (80°C)	**45**	>99	**54**	<1	90
14	**4**	$NHEt_2/LiClO_4$ 5 M	MeCN	18 h (80°C)		>99		<1	86
15	**4**	$PhSH/NEt_3$	MeOH	18 h (r.t.)	**46**	>99	**55**	<1	95
16	**4**	$PhSH/LiClO_4$ 2.5 M	MeCN	18 h (80°C)		>99		<1	87
17	**4**	$LiAlH_4$	pentane	2 h (r.t.)	**47**	>99	**56**	<1	95

Scheme 2



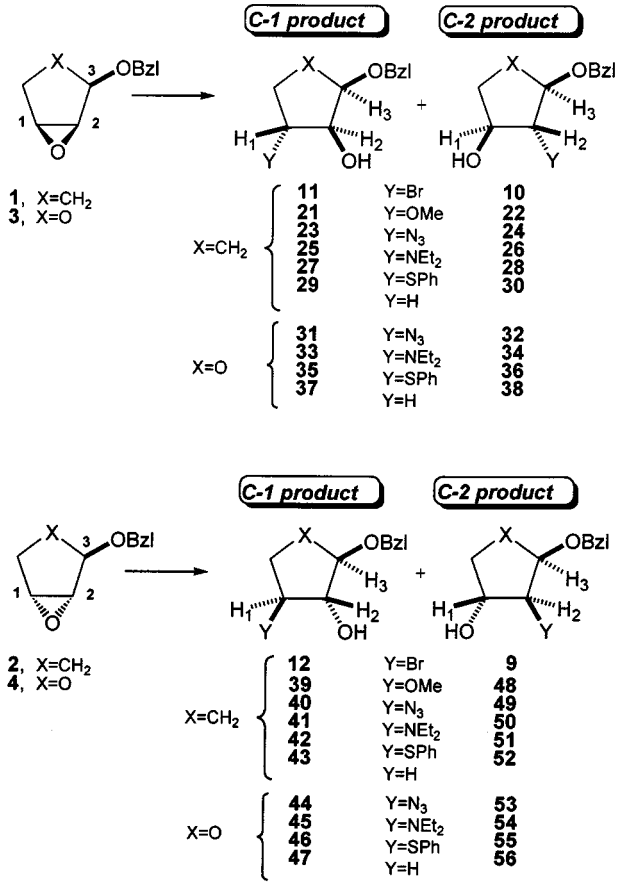
ence of benzyl alcohol afforded the *trans* selenide **17**.[8] Oxidation of **17** with H_2O_2 followed by *syn*-elimination in the presence of pyridine[9] afforded olefin **18**. While the reaction of **18** with *m*-CPBA afforded a complex, synthetically useless mixture, the use of peroxybenzimidic acid (PBIA) (prepared in situ from benzonitrile and H_2O_2)[10] afforded a 21:79 mixture of the two diastereoisomeric epoxides *cis* **3** and *trans* **4**, which could be separated by flash chromatography.[11] A complementary stereochemical result favoring the *cis* epoxide **3** (epoxide *cis* **3**/epoxide *trans* **4** = 76:24) was achieved upon base-catalyzed cyclization (aqueous NaOH) of the crude mixture of bromohydrins **19** and **20**, obtained from the reaction of olefin **18** with NBS in THF/H_2O (Scheme 3).[12]

Scheme 3



Epoxides **1**−**4** were subjected to ring-opening reactions with some representative nucleophiles (MeOH, $NHEt_2$, N_3^-, PhSH, H^-), both under standard non-chelating conditions (reactions carried out with or without classic H-acid catalysis), and under chelating conditions (reactions carried out in the presence of a metal salt or other metallic species).[13] The relative amounts of the two regioisomeric products (*C-1* and *C-2 products*, Scheme 4 and Tables 1 and 2) obtained in each case were determined by GC and/or by accurate ^{1}H-NMR examination of the crude reaction products by integration of the easily discernible signals of the H_1, H_2, and/or H_3 protons of both regioisomers (when present). In the case of epoxides **1** and **2**, acetylation of the crude reaction mixtures made it possible to determine the relative amounts of the two regioisomers more accurately.

Scheme 4



Discussion

The regioselectivity observed in the ring-opening reactions of both the *cis* epoxides **1** and **3** is strongly influenced by the reaction conditions and by the type of nucleophile (Table 1). The consistent (80−93%) C-1 selectivity observed in the ring-opening reactions carried out under standard conditions can be fully rationalized in terms of a preferential attack of the nucleophile at the oxirane C(1) carbon, which is less influenced by the unfavorable electron-withdrawing inductive effect of the nearby ether (OBzl group, epoxide **1**) or acetal functionality (epoxide **3**) (Scheme 5). In this respect, it is somewhat surprising that these reactions are not completely C-1 regioselective. Evidently, some unfavorable factors are associated with the ring-opening process at C(1), such as an increase in steric repulsion between the former oxirane oxygen and the vicinal OBzl group, as tenta-

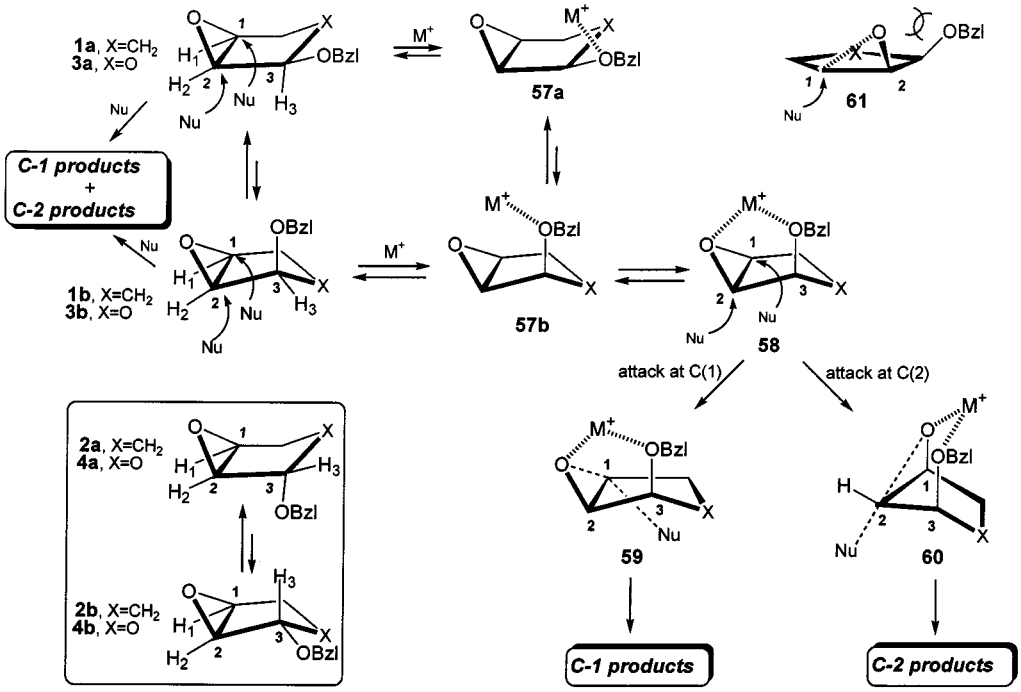
tively shown in structure **61** (X = CH_2, O, Scheme 5). These unfavorable factors lead to attack at the less electronically favored C(2) oxirane position, particularly with the strongest nucleophiles ($NHEt_2$ and PhSH, Table 1).

When the same reactions were repeated in the presence of a metal ion (chelating conditions) in a polar aprotic solvent (MeCN), an increase in C-2 selectivity was observed in most cases,[13] whereas on the basis of previous results obtained with structurally similar substrates,[3a][3b][3c][3d][3e][3f][3g][3h] an increase in C-1 selectivity might have been expected. This means that the nucleophilic attack at the oxirane C(2) carbon of the chelated bidentate structure **58** (X = CH_2, O, Scheme 5), which is hypothesized as an intermediate of the ring-opening process under chelating conditions, is somewhat favored under these conditions, as a consequence of the stereoelectronic effects connected with the ring-opening process of such chelated structures.[3a][3b][3c][3d][3e][3f][3g] Actually, a detailed examination of the chelated bidentate structure **58** (X = CH_2, O) indicates that nucleophilic attack on the oxirane carbon C(1), which is favored by the inductive effect of the substituent, leads to a reasonably stable five-membered ring −C(2)−C(3)−O−M−O− (structure **59**, X = CH_2, O), although the bonds and lone pairs may be eclipsed. On the other hand, nucleophilic attack at C(2) of **58** (X = CH_2, O), even though it is disfavored by the inductive electron-withdrawing effect of the substituent, leads to a chair-like six-membered ring −C(1)−C(2)−C(3)−O−M−O− (structure **60**, X = CH_2, O), in which the bonds and lone pairs are staggered. This makes the oxirane C(2) carbon of **58**, and hence that of **1** and **3**, more reactive under chelating conditions than under standard ones. As a consequence, under chelating conditions, a balance is struck between the electronic [favoring nucleophilic attack at C(1)] and stereoelectronic factors [favoring nucleophilic attack at C(2)]. This accounts for the observed regiochemical results, which are characterized overall by an unusual increase in C-2 selectivity (Table 1).[4][14] Consistent with this rationalization is the fact that with both the epoxides **1** and **3**, higher C-2 selectivity under chelating conditions is observed when strong nucleophiles, such as PhSH or H^- (from $LiAlH_4$) (entries 9, 10, 17, and 18, Table 1) are used, because of their lower sensitivity to the electronic effects of substituents. Analogous behaviour has been observed in similar cyclohexane- and tetrahydropyran-derived oxirane systems.[3a][3b][3c][3d][3e][3f][3g] It is notable that in the case of the $LiAlH_4$ reduction of **1** and **3**, which gives the highest C-2 selectivity, the use of a crown ether (standard conditions)[13] markedly increases the C-1 selectivity (entries 10, 11, 18, and 19, Table 1).[15]

The results obtained with the *trans* epoxides **2** and **4** showed an interesting, from a synthetic point of view, complete C-1 selectivity which turned out to be totally insensitive to the conditions of the ring-opening (Table 2). In this respect, the regiochemical behavior of the *trans* epoxides **2** and **4**, which is completely determined by the inductive electron-withdrawing effect of the substituent, is in agreement with previous results obtained for other *trans* oxirane systems.[3a][3b][3c][3d][3e][3f][3g]

In conclusion, the metal salt ($LiClO_4$) promoted ring-opening of functionalized 1,2-epoxides appears to be a useful tool for controlling the regioselectivity of the process. In the present case of *cis* epoxides **1** and **3**, this simple methodology makes it possible to obtain some of the correspond-

Scheme 5



ing *C-2 products*, which would otherwise be difficult to synthesize. This could be of some interest, particularly in the case of epoxide **3** (which is also the more C-2 selective under chelating conditions), considering the close similarity of this epoxide and its ring-opened products to natural glycofuranosides and related compounds.

Structures, Configurations, and Conformations

The structures and relative configurations of epoxides *cis* **1** and *trans* **2** were unequivocally established by their method of preparation, on the basis of the known heteroatom-directed peracid epoxidation.[6d] As for epoxides **3** and **4**, their relative configuration was determined only by examination of the IR spectra in dilute CCl_4 solution of the alcohols (**37** and **38** from **3**, and **47** from **4**) obtained upon their reduction with $LiAlH_4$. Both alcohols **37** and **38** show the presence of a band characteristic of an OH···Q interaction: at $\nu = 3570\ cm^{-1}$ (1,2-OH···O) in **37** and at $\nu = 3551\ cm^{-1}$ (1,3-OH···O) in **38** (Table 3). In contrast, alcohol **47** shows the presence of an intense band at $\nu = 3624\ cm^{-1}$, characteristic of a free (non-bonded) OH group (Table 3).[4][16] Bearing in mind that following the reduction of an epoxide, the configuration of the alcohol(s) obtained corresponds to that of the starting epoxide, on the basis of these results we can assign the *cis* configuration to epoxide **3** and the *trans* configuration to the diastereoisomeric epoxide **4**.

The conformational equilibria of the epoxides **1** and **2** were determined by examination of the signal of the proton H_3, α to the OBzl group, in the ^{1}H-NMR spectra of these compounds. The larger coupling constant in **1** ($J = 7.4$ Hz) and the smaller value in **2** ($J = 5.4$ Hz) indicate that this proton is pseudoaxial in the former and pseudoequatorial in the latter. Thus, both **1** and **2** preferentially adopt the boat conformations **1a** and **2a** (Scheme 5).[17][18]

The relative structures of the regioisomeric pairs of *C-1* and *C-2 products* obtained from the ring-opening reactions of epoxides *cis* **1** and **3**, as well as of the *C-1 products* obtained from *trans* epoxides **2** and **4**, were unequivocally assigned on the basis of the usual considerations, as in previous examples.[3a-f][4]

As previously observed for other related cyclopentane derivatives,[4] the IR spectra in dilute CCl_4 solution of the *C-1* and *C-2 products* from the *cis* epoxides **1** and **3** (bromohydrins **10**−**11** and compounds **21**−**38**), the *C-1 products* from the *trans* epoxides **2** and **4** (bromohydrin **12** and compounds **39**−**47**), and the *C-2 product* from the *trans* epoxide **2** (bromohydrin **9**) (Scheme 4) show three characteristic patterns, which, on the basis of appropriate considerations, can be correlated to three of the four possible 1,2-*trans* relationships (Scheme 6 and Table 3):[4][16][20]

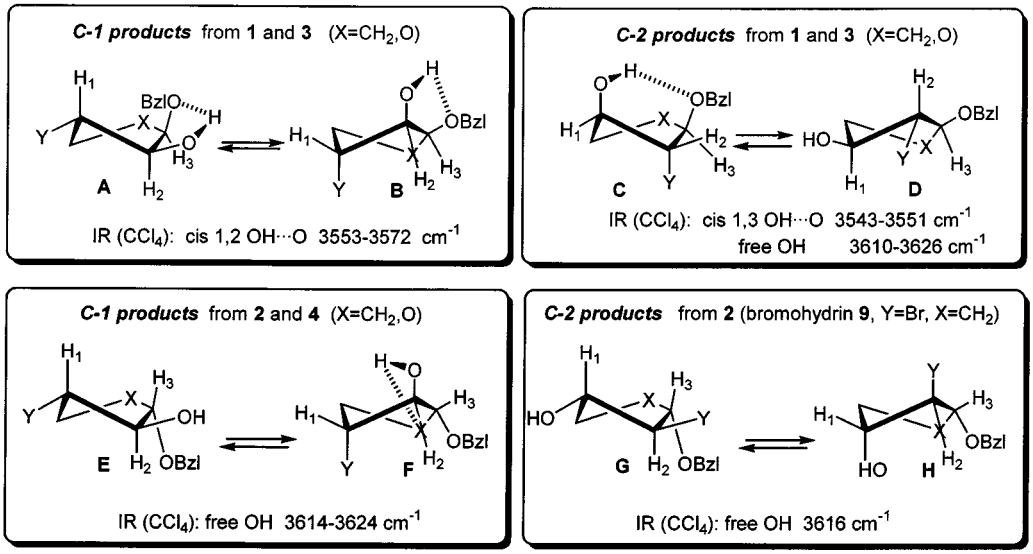
(a) *C-1 products* from *cis* epoxides **1** and **3**: The presence of an intense band at $\nu = 3553-3572\ cm^{-1}$ due to a *cis*

Table 3. Spectroscopic data for bromohydrins **9**−**12** and compounds **21**−**47**[a]

compd.	^{1}H NMR δ			IR (CCl_4) (OH stretching), cm^{-1}		
	H_1 ($W_{1/2}$,Hz)[b-d]	H_2 ($W_{1/2}$,Hz)[b-d]	H_3 ($W_{1/2}$,Hz)[e]	1,3-OH···O	1,2-OH···O	free OH
9	[f]	4.50 (18.0)[b][g]	[f]	–	–	3616
10	4.30 (17.0)[d][g]	[f]	[f]	3543[n]	–	3610
11	[f]	[f]	[f]	–	3553[o]	–
12	3.78 (19.6)[b][h]	4.23 (17.4)[d][i]	3.93 (21.8)[j]	–	–	3610[o]
21	[f]	3.68 (13.3)[d][g]	[f]	–	3552	–
23	[f]	[f]	[f]	–	3560	–
24	[f]	[f]	3.96 (14.0)[g]	3543[n]	–	3622[n]
25	3.01 (21.2)[c][h]	3.94 (12.8)[d][i]	3.83 (14.8)[j]	–	3558	–
26	[f]	3.04 (12.8)[c][j]	[f]	3545[n]	–	3616[n]
27	3.58 (19.1)[c][g]	[f]	[f]	–	3560	–
28	4.09 (17.7)[d][g]	3.59 (9.0)[c][i]	3.90 (13.3)[g]	3543[n]	–	3616[n]
29	–	4.09 (14.1)[d][g]	3.81 (17.6)[h]	–	3572	–
30	4.26 (17.2)[d][g]	–	4.09 (13.8)[h]	3549[n]	–	3624[p]
31	3.64 (16.6)[c][j]	3.93 (14.3)[d][g]	5.05 ($J = 4.4$)[k]	–	3564	–
32	[f]	[f]	5.04[l]	3547	–	3626[p]
33	3.31 (21.0)[c][j]	3.77 (16.0)[d][j]	5.05 ($J = 4.7$)[k]	–	3566	–
34	4.28 (14.6)[d][h]	3.26 (8.3)[c][j]	5.07 ($J = 1.5$)[k]	3549[n]	–	3622[n]
35	3.64 (14.2)[c][j]	4.11 (14.2)[d][g]	5.13 ($J = 4.5$)[k]	–	3562	–
36	4.24 (21.7)[d][g]	3.75[c][l]	5.16[l]	3543	–	3616[p]
37	–	4.25 (17.8)[d][g]	5.02 ($J = 4.4$)[k]	–	3570	–
38	4.35 (17.7)[d][g]	–	5.27 ($J = 4.3$)[k]	3551[o]	–	–
39	3.74 (21.2)[c][h]	3.99 (19.1)[d][j]	3.54 (21.2)[h]	–	–	3614
40	3.61 (17.5)[c][g]	3.97 (14.0)[d][i]	3.79 (17.5)[g]	–	–	3618
41	2.95 (18.5)[c][g]	3.92 (14.8)[d][j]	3.77 (14.8)[g]	–	–	3610[n]
42	3.26 (17.4)[c][m]	3.97 (15.2)[d][j]	3.83 (15.8)[g]	–	–	3614
43	–	4.16 (17.5)[d][g]	3.76 (17.5)[g]	–	–	3624
44	[f]	4.24 (5.1)[d][g]	4.99[l]	–	3591[p]	3622
45	3.26 (22.0)[c][h]	4.19 (7.6)[d][j]	4.96 ($J = 1.1$)[k]	–	–	3616
46	3.55 (13.8)[c][h]	4.25 (9.5)[d][g]	5.03[l]	–	3593[p]	3620[n]
47		4.21 (8.5)[d][j]	4.92[l]	–	3599[p]	3624[n]

[a] Compound **22** (Scheme 4), which is produced in insignificant amounts in the methanolysis reactions of epoxide **1**, is not included. Compounds **48**−**56** (Scheme 4) are not obtained in the ring-opening reactions of epoxides **2** and **4**. – [b] CHBr. – [c] CHY. – [d] CHOH. – [e] CHOBzl (Schemes 1 and 5). – [f] The signal overlaps with other signals. – [g] Multiplet. – [h] Doublet of doublet of doublets. – [i] Triplet. – [j] Doublet of doublets. – [k] Doublet. – [l] Singlet. – [m] Quartet. – [n] Strong band. – [o] Broad band. – [p] Weak band.

Scheme 6



1,2-interaction between the two adjacent groups (OH and OBzl), possible in both conformations **A** and **B**.

(b) *C-2 products* from *cis* epoxides **1** and **3**: The presence of an intense band at $\nu = 3543-3551$ cm^{-1} attributable to a *cis* 1,3-OH···O interaction, possible only in conformation **C** with the relevant groups (OH and OBzl) in a 1,3-dipseudoaxial relationship. A band at $\nu = 3610-3626$ cm^{-1}, characteristic of a free OH, is also present, indicating a minor contribution from conformer **D** with the OH and OBzl groups in a 1,3-dipseudoequatorial relationship.

(c) *C-1 products* from *trans* epoxides **2** and **4**, and *C-2 products* from *trans* epoxide **2** (bromohydrin **9** is the sole representative of this class of compounds): The presence of a single band at $\nu = 3614-3624$ cm^{-1}, attributable to a free OH group. In these compounds, the 1,2- or 1,3-*trans* relationship between the OH and the OBzl groups does not allow any type of interaction (i.e. hydrogen bond) in either of the two possible conformations **E** or **F** (*C-1 products*) and **G** or **H** (*C-2 products*). In fact, an additional weak band at $\nu = 3591-3599$ cm^{-1} is observed in some *C-1 products* derived from epoxide **4** (compounds **44**, **46** and **47**, Table 3), due to a 1,2-OH···O interaction between the OH group and the endocyclic oxygen, which is only possible in conformation **F**, as shown in Scheme 6.[20]

Financial support from the *Consiglio Nazionale delle Ricerche (CNR)* and the *Ministero della Universita e della Ricerca Scientifica e Tecnologica (MURST)*, Roma, is gratefully acknowledged.

Experimental Section

General Methods: For general experimental details and procedures see ref.[3a]. ^{1}H- and ^{13}C-NMR spectra of $CDCl_3$ solutions were recorded at 200 and 50 MHz, respectively, with a Bruker AC 200 spectrometer. GC analyses were performed on a Perkin-Elmer 8420 apparatus (FI detector) with a 30 m × 0.25 mm (i.d.) × 0.25 μm (film thickness) DB-WAX fused silica capillary column. In all cases, the injector and detector temperatures were 250°C and a 2 ml/min nitrogen flow rate was employed.

2-Cyclopenten-1-ol (**5**): A 1 M DIBAL-H solution in hexane (60 ml) was added dropwise at 0−5°C to a stirred solution of 2-cyclopenten-1-one (4.10 g, 50.0 mmol) in anhydrous benzene (75 ml). After stirring for 2 h, MeOH was added at the same temperature. Concentration of the filtered organic solution afforded a crude liquid product (4.0 g) essentially consisting of alcohol **5**, which was directly utilized in the next step without further purification.[5]

3-(Benzyloxy)cyclopentene (**8**): A solution of alcohol **5** (0.84 g, 10.0 mmol) in anhydrous THF (10 ml) was added to a stirred suspension of NaH (0.60 g of an 80% dispersion in mineral oil, 20.0 mmol) in anhydrous THF (20 ml) containing benzyl bromide (1.2 ml, 10.5 mmol) and the resulting mixture was stirred at 50°C for 18 h. After cooling, dilution with diethyl ether, and addition of water (caution!), concentration of the washed (saturated aqueous $NaHCO_3$) organic phase afforded a crude liquid product (1.48 g), which was filtered through a short silica gel column. Elution with petroleum ether afforded pure olefin **8** (1.23 g, 71% yield) as a liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.27−7.37 (m, 5 H), 5.98 (m, 2 H), 4.69 (m, 1 H), 4.55 (ABdd, 2 H, *J* = 11.7 Hz), 1.79−2.62 (m, 4 H). − $C_{12}H_{14}O$ (174.2): calcd. C 82.71, H 8.09; found C 82.60, H 8.15.

Oxidation of Olefin **8** *with m-CPBA:* A solution of olefin **8** (0.35 g, 2.0 mmol) in CH_2Cl_2 (15 ml) was treated at 0°C with 55% *m*-CPBA (0.75 g, 2.4 mmol) and the resulting mixture was stirred at this temperature for 3 h. Dilution with further CH_2Cl_2 and concentration of the washed (10% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, 5% aqueous NaOH, and saturated aqueous NaCl) organic phase afforded a crude product (0.35 g) consisting of a 34:66 mixture of epoxides **1** and **2** (GC), which was subjected to flash chromatography. Elution with an 85:15 mixture of hexane and AcOEt afforded pure epoxides *cis* **1** (0.10 g) and *trans* **2** (0.21 g).

rel-(1*R*,2*R*,3*S*)-*3-(Benzyloxy)-1,2-epoxycyclopentane* (**1**): Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.18−7.33 (m, 5 H), 4.56 (s, 2 H), 3.97 (ddd, 1 H, *J* = 7.4 and 0.9 Hz), 3.39 (m, 2 H), 1.98−2.08 (m, 1 H), 1.69−1.79 (m, 1 H), 1.31−1.60 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 138.79, 130.34, 128.94, 128.34, 128.26, 127.57, 72.12, 56.82, 55.78, 26.00, 24.14. − $C_{12}H_{14}O_2$ (190.2): calcd. C 75.76, H 7.41; found C 75.80, H 7.21.

rel-(1*R*,2*R*,3*R*)-*3-(Benzyloxy)-1,2-epoxycyclopentane* (**2**): Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.18−7.29 (m, 5 H), 4.44 and 4.53 (ABdd, 2 H, *J* = 11.8 Hz), 4.02 (d, 1 H, *J* = 5.4 Hz), 3.45 (dd, 2 H, *J* = 9.5 and 2.4 Hz), 1.63−1.90 (m, 3 H), 1.42−1.43 (m, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 138.74, 129.01, 128.31, 128.26, 79.34, 72.05, 57.70, 26.78, 25.88. − $C_{12}H_{14}O_2$ (190.2): calcd. C 75.76, H 7.41; found C 75.65, H 7.09.

Reaction of Olefin **8** *with NBS in THF/H_2O:* A solution of olefin **8** (0.35 g, 2.0 mmol) in a 3:1 THF/H_2O mixture (16 ml) was treated with NBS (0.41 g, 2.3 mmol) and the mixture was stirred at room temperature for 2 h. Dilution with diethyl ether and concentration of the washed (10% aqueous $Na_2S_2O_3$ and saturated aqueous NaCl) organic phase afforded a crude liquid product (0.96 g) consisting of a 67:33 mixture of bromohydrins **9** and **10**, which was subjected to flash chromatography. Elution with an 85:15 mixture of hexane and AcOEt afforded pure bromohydrins **9** (0.59 g) and **10** (0.23 g).

rel-(1*R*,2*S*,3*R*)-*3-(Benzyloxy)-2-bromo-1-cyclopentanol* (**9**): Solid, m.p. 60.5−61.5°C. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.24−7.42 (m, 5 H), 4.52 and 4.63 (ABdd, 2 H, *J* = 11.8 Hz), 4.46−4.54 (m, 1 H), 4.01−4.14 (m, 2 H), 2.26−2.39 (m, 1 H), 1.80−2.15 (m, 2 H), 1.44−1.70 (m, 1 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.5, 129.0, 128.5, 128.4, 79.4, 78.8, 72.4, 60.2, 29.4, 27.8. − $C_{12}H_{15}BrO_2$ (271.2): calcd. C 53.15, H 5.57; found C 53.39, H 5.71.

rel-(1*R*,2*S*,3*S*)-*3-(Benzyloxy)-2-bromo-1-cyclopentanol* (**10**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.40 (m, 5 H), 4.56 and 4.64 (ABdd, 2 H, *J* = 11.7 Hz), 4.37−4.22 (m, 1 H), 4.11−4.21 (m, 2 H), 2.12−2.31 (m, 2 H), 1.80−2.10 (m, 2 H); see also Table 3. − $C_{12}H_{15}BrO_2$ (271.2): calcd. C 53.15, H 5.57; found C 53.10, H 5.26. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.45 (m, 5 H), 5.19−5.23 (m, 1 H), 4.56 and 4.65 (ABdd, 2 H, *J* = 12.0 Hz), 4.13−4.15 (m, 2 H), 2.04−2.31 (m, 2 H), 2.07 (s, 3 H), 1.64−1.94 (m, 2 H). − $C_{14}H_{17}BrO_3$ (313.2): calcd. C 53.69, H 5.47; found C 53.42, H 5.34.

Base-Catalyzed Cyclization of the Mixture of Bromohydrins **9** *and* **10**: A solution of the aforementioned 67:33 crude mixture of bromohydrins **9** and **10** (0.56 g, 2.0 mmol) in anhydrous benzene (40 ml) was treated with *t*BuOK (2 × 0.25 g, 2 × 2.0 mmol) and the mixture was stirred for 2 h at room temperature. Concentration of the filtered organic solution afforded a crude liquid product (0.36 g) consisting of a 25:75 mixture of epoxides **1** and **2** (GC).

Epoxide cis **1**: A solution of olefin **5** (0.504 g, 6.0 mmol) in CH_2Cl_2 (45 ml) was treated at 0°C with 55% *m*-CPBA (2.06 g, 6.6 mmol) and the reaction mixture was stirred at this temperature for 1 h. Standard work-up afforded a crude liquid product (0.40 g, 67% yield) consisting of a 98:2 mixture of epoxy alcohols **6** and **7** (GC),[6] which, without further purification, was added to a suspension of NaH (0.24 g of an 80% dispersion in mineral oil, 8.0 mmol) in anhydrous THF (12 ml) containing benzyl bromide (0.48 ml, 4.0 mmol). The usual work-up afforded a crude liquid product (0.68 g) consisting of a 98:2 mixture of epoxides **1** and **2** (GC), which was filtered through a silica gel column. Elution with petroleum ether afforded the pure epoxide *cis* **1** (0.54 g).

Reaction of Epoxides **1** *and* **2** *with HBr/$CHCl_3$:* The following procedure is typical. A solution of the epoxide *cis* **1** (0.177 g, 0.93 mmol) in $CHCl_3$ (10 ml) was treated with 48% aqueous HBr (3 ml) and the reaction mixture was stirred at room temperature for 30 min. Concentration of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic phase afforded a crude product (0.210 g) consisting of an 86:14 mixture of bromohydrins **11** and **10** (^{1}H NMR), which was subjected to preparative TLC using a 75:25 mixture of hexane and AcOEt as eluent. Extraction of the two most intense bands (the faster moving band contained **11**) afforded pure **10** (0.018 g) and *rel*-(1*R*,2*R*,5*R*)-*2-(benzyloxy)-5-bromo-1-cyclopentanol* (**11**) (0.12 g) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.40 (m, 5 H), 4.50 and 4.60 (ABdd, 2 H, *J* = 11.5 Hz), 4.13−4.19 (m, 3 H), 2.60−2.43 (m, 1 H), 2.06−2.23 (m, 1 H), 2.02−1.71 (m, 2 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.1, 129.2, 128.7, 128.4, 79.7, 79.1, 72.5, 54.3, 32.3, 28.2. − $C_{12}H_{15}BrO_2$ (271.2): calcd. C 53.15, H 5.57; found C 53.01, H 5.28. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.24−7.39 (m, 5 H), 5.17 (t, 1 H, *J* = 5.1 Hz), 4.49 (s, 2 H), 4.19−4.35 (m, 2 H), 2.42−2.61 (m, 1 H), 2.11 (s, 3 H), 1.77−2.23 (m, 3 H). − $C_{14}H_{17}BrO_3$ (313.2): calcd. C 53.69, H 5.47; found C 53.81, H 5.77.

The crude reaction product (0.185 g) from the epoxide *trans* **2**, consisting of bromohydrin **12**, was filtered through a silica gel column. Elution with an 8:2 mixture of hexane and AcOEt afforded pure *rel*-(1*R*,2*S*,5*R*)-*2-(benzyloxy)-5-bromo-1-cyclopentanol* (**12**) (0.13 g) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.24−7.38 (m, 5 H), 4.59 (s, 2 H), 4.23 (t, 1 H, *J* = 6.2 Hz), 3.93 (dd, 1 H, *J* = 16.2 and 7.5 Hz), 3.78 (ddd, 1 H, *J* = 7.9 and 5.9 Hz), 1.76−2.36 (m, 4 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.6, 129.1, 128.4, 85.4, 83.2, 72.2, 53.3, 32.3, 29.0. − $C_{12}H_{15}BrO_2$ (271.2): calcd. C 53.15, H 5.57; found C 53.49, H 5.73. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.35 (m, 5 H), 5.41 (dd, 1 H, *J* = 4.0 and 2.7 Hz), 4.52 and 4.64 (ABdd, 2 H, *J* = 11.9 Hz), 4.06 (ddd, 1 H, *J* = 10.6, 6.2 and 3.8 Hz), 3.84 (td, 1 H, *J* = 5.8 and 2.7 Hz), 2.16−2.31 (m, 2 H), 2.07 (s, 3 H), 1.96−2.10 (m, 2 H). − $C_{14}H_{17}BrO_3$ (313.2): calcd. C 53.69, H 5.47; found C 53.70, H 5.81.

trans-2-(Benzyloxy)-3-(phenylselenyl)tetrahydrofuran (**17**): Following a previously described procedure,[8] treatment of a solution of PhSeCl (2.10 g, 11.0 mmol) in anhydrous THF (50 ml) with 2,3-dihydrofuran (0.70 g, 10.0 mmol) and a mixture of benzyl alcohol (1.83 g, 17.0 mmol) and NEt_3 (1.51 g, 15.0 mmol) afforded a crude liquid product (2.8 g) consisting of crude selenide **17** (^{1}H NMR), which was purified by filtration through a silica gel column. Elution with a 95:5 mixture of petroleum ether and AcOEt afforded pure **17** (2.5 g, 76% yield) as a liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.46−7.55 (m, 2 H), 7.19−7.36 (m, 8 H), 5.23 (s, 1 H), 4.43 and 4.67 (ABdd, 2 H, *J* = 11.8 Hz), 3.94−4.17 (m, 2 H), 3.77 (ddd, 1 H, *J* = 7.7, 4.3 and 0.8 Hz), 2.45−2.62 (m, 1 H), 1.84−2.00 (m, 1 H).

2-(Benzyloxy)-2,5-dihydrofuran (**18**): A solution of selenide **17** (0.30 g, 0.90 mmol) in CH_2Cl_2 (4.0 ml) and pyridine (0.3 ml) was treated at 0°C with 16% aqueous H_2O_2 (0.7 ml) and the mixture was stirred at this temperature for 12 h. Dilution with CH_2Cl_2 and concentration of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic solution afforded a liquid product (0.21 g), which was filtered through a silica gel column. Elution with a 95:5 mixture of petroleum ether and AcOEt afforded pure olefin **18** (0.12 g, 76% yield) as a liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.24−7.44 (m, 5 H), 6.25−6.30 (m, 1 H), 5.95−5.98 (m, 1 H), 5.81−5.87 (m, 1 H, $W_{1/2}$ = 10.1 Hz), 4.57 and 4.75 (ABdd, 2 H, *J* = 11.8 Hz), 4.71−4.82 (m, 1 H), 4.55−4.69 (m, 1 H). − $C_{11}H_{12}O_2$ (176.2): calcd. C 74.97, H 6.86; found C 74.76, H 7.05.

Oxidation of Olefin **18** *with Peroxybenzimidic Acid:* Following a previously described procedure,[10] to a vigorously stirred suspension of K_2CO_3 (0.142 g) in MeOH (3.0 ml) containing olefin **18** (1.0 g, 5.7 mmol) and benzonitrile (0.88 g, 8.5 mmol) at 15−20°C, 35% aqueous H_2O_2 (1.40 ml, 14.2 mmol) was added dropwise. The reaction mixture was stirred at this temperature for 1 h, then at

40°C for 30 min. A small amount of Pd/C was added at this temperature in order to destroy the excess H_2O_2. Dilution with $CHCl_3$ and concentration of the washed (saturated aqueous NaCl) organic solution afforded a crude product, which was repeatedly extracted with petroleum ether. Evaporation of the combined organic extracts afforded a crude liquid product (1.16 g) consisting of a 21:79 mixture of epoxides *cis* **3** and *trans* **4** (^{1}H NMR), which was subjected to flash chromatography. Elution with an 8:2 mixture of hexane and AcOEt afforded pure epoxides *cis* **3** (0.097 g) and *trans* **4** (0.72 g).

D,L-Benzyl-2,3-dehydro-α-erythrofuranoside (**3**): Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.14−7.47 (m, 5 H), 5.08 (s, 1 H), 4.57 and 4.81 (ABdd, 2 H, *J* = 12.0 Hz), 3.70 and 4.15 (ABdd, 2 H, *J* = 10.8 Hz), 3.72 and 4.17 (ABdd, 2 H, *J* = 10.8 Hz), 3.64 (s, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 138.12, 129.09, 128.70, 128.51, 101.22, 71.40, 67.62, 56.56, 55.38. − $C_{11}H_{12}O_3$ (192.2): calcd. C 68.73, H 6.29; found C 68.59, H 6.35.

D,L-Benzyl-2,3-dehydro-β-erythrofuranoside (**4**): Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.24−7.41 (m, 5 H), 5.15 (s, 1 H), 4.54 and 4.77 (ABdd, 2 H, *J* = 11.5 Hz), 3.85 and 4.02 (ABdd, 2 H, *J* = 10.5 Hz), 3.74 (dd, 2 H, *J* = 6.8 and 2.9 Hz). − ^{13}C NMR ($CDCl_3$): δ = 138.14, 129.03, 128.86, 128.55, 128.39, 127.89, 100.85, 70.21, 66.46, 56.67, 53.85. − $C_{11}H_{12}O_3$ (192.2): calcd. C 68.73, H 6.29; found C 68.61, H 6.54.

Reaction of Olefin **18** *with NBS in THF/H_2O, Followed by Treatment with Aqueous NaOH:* A solution of olefin **18** (0.176 g, 1.0 mmol) in 3:1 THF/H_2O (10 ml) was treated with NBS (0.196 g, 1.1 mmol) and the mixture was left for 15 min in the dark at room temperature. A few drops of an ethanolic solution of phenolphthalein were added and the mixture was titrated with aqueous 1 N NaOH. Dilution with water, extraction with diethyl ether, and concentration of the washed (saturated aqueous NaCl) ethereal extracts afforded a crude liquid product (0.15 g) consisting of a 76:24 mixture of epoxides *cis* **3** and *trans* **4** (GC), which was separated by flash chromatography as described above.

Acid Methanolysis of Epoxides **1** *and* **2**: The following procedure is typical. A solution of the epoxide *cis* **1** (0.095 g, 0.50 mmol) in a 0.2 N H_2SO_4 solution in anhydrous MeOH (10 ml) was stirred at room temperature for 30 min. Dilution with saturated aqueous $NaHCO_3$, extraction with diethyl ether, and concentration of the washed (saturated aqueous NaCl) ethereal extracts afforded a crude liquid product (0.10 g) consisting of a 93:7 mixture of methoxy alcohols **21** and **22** (GC), which was subjected to preparative TLC using a 9:1 mixture of hexane and AcOEt as eluent. Extraction of the most intense band afforded pure *rel*-(1*R*,2*S*,5*S*)-*2-(benzyloxy)-5-methoxy-1-cyclopentanol* (**21**) (0.070 g) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.34 (m, 5 H), 4.50 and 4.60 (ABdd, 2 H, *J* = 11.6 Hz), 4.13−4.92 (m, 2 H), 3.65−3.72 (m, 1 H, $W_{1/2}$ = 13.3 Hz), 3.36 (s, 3 H), 1.67−2.22 (m, 3 H), 1.41−1.50 (m, 1 H); see also Table 3. − $C_{13}H_{18}O_3$ (222.3): calcd. C 70.24, H 8.16; found C 70.42, H 8.01. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.36 (m, 5 H), 5.00−5.04 (m, 1 H), 4.99 (s, 2 H), 4.07 (q, 1 H, *J* = 6.0 Hz), 3.77−3.89 (m, 1 H), 3.35 (s, 3 H), 2.10 (s, 3 H), 1.76−2.16 (m, 4 H). − $C_{15}H_{20}O_4$ (264.3): calcd. C 68.16, H 7.62; found C 68.33, H 7.29.

The crude reaction product from the epoxide *trans* **2** was found to consist of practically pure *rel*-(1*R*,2*R*,5*S*)-*2-(benzyloxy)-5-methoxy-1-cyclopentanol* (**39**) (0.105 g) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.22−7.37 (m, 5 H), 4.54 and 4.58 (ABdd, 2 H, *J* = 11.8 Hz), 3.99 (dd, 1 H, *J* = 12.4 and 6.2 Hz), 3.74 (ddd, 1 H, *J* = 12.6, 6.4 and 2.5 Hz), 3.54 (ddd, 1 H, *J* = 12.2, 6.3 and 2.5 Hz), 3.36 (s, 3 H), 1.83−2.03 (m, 2 H), 1.63−1.80 (m, 2 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.9, 129.0, 128.4, 128.3, 85.7, 83.9, 82.8, 72.1, 57.7, 27.1, 26.6. − $C_{13}H_{18}O_3$ (222.3): calcd. C 70.24, H 8.16; found C 70.31, H 8.44. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.23−7.34 (m, 5 H), 5.15 (t, 1 H, *J* = 2.7 Hz), 4.55 and 4.62 (ABdd, 2 H, *J* = 12.2 Hz), 3.81 (ddd, 1 H, *J* = 5.4 and 3.1 Hz), 3.66 (m, 1 H), 3.36 (s, 3 H), 2.06 (s, 3 H), 1.88−1.90 (m, 4 H). − $C_{15}H_{20}O_4$ (264.3): calcd. C 68.16, H 7.62; found C 68.42, H 7.35.

Methanolysis of Epoxides **1** *and* **2** *in the Presence of $LiClO_4$ − General Procedure:* The epoxide (0.25 mmol) was added to a 17 M $LiClO_4$ solution in anhydrous MeOH (1.0 ml) and the reaction mixture was stirred at 80°C for 24 h. Dilution with diethyl ether and concentration of the washed (saturated aqueous NaCl) organic solution afforded a crude product, which was analyzed by GC and ^{1}H-NMR spectroscopy (Tables 1 and 2).

Azidolysis of Epoxides **1−4** *with NaN_3/NH_4Cl:* The following procedure is typical. A solution of epoxide **1** (0.19 g, 1.0 mmol) in 8:1 MeOH/H_2O (10 ml) was treated with NaN_3 (0.325 g, 5.0 mmol) and NH_4Cl (0.123 g, 2.3 mmol) and the reaction mixture was stirred at 80°C for 18 h. Dilution with diethyl ether and concentration of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic solution afforded a crude liquid product (0.271 g) consisting of a 93:7 mixture of azido alcohols **23** and **24** (GC), which was subjected to preparative TLC using a 2:1 mixture of petroleum ether and diethyl ether as eluent. Extraction of the two most intense bands (the faster moving band contained **23**) afforded pure azido alcohols **23** (0.15 g) and **24** (0.010 g).

rel-(1*R*,2*S*,5*S*)-*2-Azido-5-(benzyloxy)-1-cyclopentanol* (**23**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.40 (m, 5 H), 4.48 and 4.60 (ABdd, 2 H, *J* = 11.9 Hz), 3.79−4.04 (m, 3 H), 1.67−2.24 (m, 3 H), 1.45−1.62 (m, 1 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.2, 129.1, 128.6, 128.4, 79.2, 72.2, 66.9, 27.1, 26.6, 24.2. − $C_{12}H_{15}N_3O_2$ (233.3): calcd. C 61.79, H 6.48, N 18.00; found C 61.54, H 6.28, N 18.15. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.24−7.37 (m, 5 H), 4.83 (dd, 1 H, *J* = 7.0 and 4.7 Hz), 4.47 and 4.50 (ABdd, 2 H, *J* = 11.9 Hz), 4.05−4.16 (m, 2 H), 2.10−2.29 (m, 1 H), 2.12 (s, 3 H), 1.74−2.07 (m, 2 H), 1.46−1.58 (m, 1 H). − $C_{14}H_{17}N_3O_3$ (275.3): calcd. C 61.08, H 6.22, N 15.25; found C 61.39, H 6.51, N 15.60.

rel-(1*R*,2*S*,3*S*)-*2-Azido-3-(benzyloxy)-1-cyclopentanol* (**24**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.40 (m, 5 H), 4.55 (s, 2 H), 3.90−4.03 (m, 1 H), 3.43−3.86 (m, 2 H), 1.92−2.10 (m, 2 H), 1.25−1.90 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 138.3, 129.1, 128.5, 128.4, 82.6, 76.0, 73.2, 72.2, 66.0, 62.6, 30.8, 28.0. − $C_{12}H_{15}N_3O_2$ (233.3): C 61.79, H 6.48, N 18.00; found C 61.59, H 6.77, N 18.21.

The crude reaction product (0.106 g) from the epoxide *trans* **2** (0.50 mmol) was found to consist of essentially pure *rel*-(1*R*,2*R*,5*S*)-*2-azido-5-(benzyloxy)-1-cyclopentanol* (**40**) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.24−7.46 (m, 5 H), 4.55 and 4.57 (ABdd, 2 H, *J* = 12.0 Hz), 3.97 (t, 1 H, *J* = 6.6 Hz), 3.72−3.85 (m, 1 H), 3.56−3.67 (m, 1 H), 1.92−2.10 (m, 2 H), 1.66−1.88 (m, 2 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.7, 129.2, 128.4, 83.8, 72.4, 66.0, 64.7, 27.4, 26.6. − $C_{12}H_{15}N_3O_2$ (233.3): calcd. C 61.79, H 6.48, N 18.00; found C 61.89, H 6.51, N 17.94. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.35 (m, 5 H), 5.11 (t, 1 H, *J* = 3.7 Hz), 4.54 and 4.58 (ABdd, 2 H, *J* = 12.0 Hz), 3.83−3.89 (m, 1 H), 3.74−3.80 (m, 1 H), 2.07 (s, 3 H), 1.85−2.01 (m, 4 H). − ^{13}C NMR ($CDCl_3$): δ = 170.6, 138.6, 129.0, 128.3, 83.1, 82.7, 71.8, 65.8, 29.7, 28.7, 21.7. − $C_{14}H_{17}N_3O_3$ (275.3): calcd. C 61.08, H 6.22, N 15.25; found C 61.32, H 6.00, N 15.06.

The crude reaction product (0.112 g) from the epoxide *cis* **3** (0.50 mmol), consisting of an 84:16 mixture of azido alcohols **31** and **32** (GC), was subjected to preparative TLC using an 8:2 mixture of petroleum ether and diethyl ether as eluent. Extraction of the two most intense bands (the faster moving band contained **31**) afforded pure azido alcohols **31** (0.070 g) and **32** (0.012 g).

D,L-Benzyl-3-deoxy-3-(β-azido)-α-erythrofuranoside (**31**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.23−7.35 (m, 5 H), 5.05 (d, 1 H, *J* = 4.4 Hz), 4.50 and 4.75 (ABdd, 2 H, *J* = 11.6 Hz), 4.07−4.15 (m, 2 H), 3.89−3.97 (m, 1 H), 3.64 (dd, 1 H, *J* = 4.5 Hz); see also Table 3. − $C_{11}H_{13}N_3O_3$ (235.2): calcd. C 56.16, H 5.57, N 17.85; found C 56.38, H 5.24, N 17.62. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.23−7.39 (m, 5 H), 5.34 (d, 1 H, *J* = 4.3 Hz), 4.83 (dd, 1 H, *J* = 6.3 and 4.4 Hz), 4.48 and 4.73 (ABdd, 2 H, *J* = 11.9 Hz), 4.34 (ddd, 1 H, *J* = 7.6 and 5.2 Hz), 4.21 (dd, 1 H, *J* = 9.2 and 7.7 Hz), 3.71 (dd, 1 H, *J* = 9.2 and 4.9 Hz), 2.11 (s, 3 H). − $C_{13}H_{15}N_3O_4$ (277.3): calcd. C 56.31, H 5.45, N 15.14; found C 56.11, H 5.82, N 15.33.

D,L-Benzyl-2-deoxy-2-(β-azido)-α-erythrofuranoside (**32**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.18−7.33 (m, 5 H), 5.04 (s, 1 H), 4.46 and 4.70 (ABdd, 2 H, *J* = 11.6 Hz), 4.18−4.25 (m, 2 H), 3.86−3.92 (m, 2 H); see also Table 3. − $C_{11}H_{13}N_3O_3$ (235.2): C 56.16, H 5.57, N 17.85; found C 56.31, H 5.84, N 18.07. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.38 (m, 5 H), 5.06 (ddd, 1 H, *J* = 5.1 and 2.1 Hz), 5.04 (s, 1 H), 4.51 and 4.78 (ABdd, 2 H, *J* = 11.8 Hz), 4.38 (dd, 1 H, *J* = 10.0 and 6.8 Hz), 4.02 (s, 1 H), 3.90 (dd, 1 H, *J* = 10.0 and 5.1 Hz), 2.10 (s, 3 H). − $C_{13}H_{15}N_3O_4$ (277.3): C 56.31, H 5.45, N 15.14; found C 56.46, H 5.70, N 14.89.

The crude reaction product (0.110 g) from the epoxide *trans* **4** (0.50 mmol) was found to consist of essentially pure *D,L-benzyl-3-deoxy-3-(β-azido)-β-erythrofuranoside* (**44**) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.36 (m, 5 H), 4.99 (s, 1 H), 4.49 and 4.74 (ABdd, 2 H, *J* = 11.9 Hz), 4.29 (ddd, 1 H, *J* = 12.0 and 2.3 Hz), 4.20−4.28 (m, 1 H), 3.91−3.83 (m, 2 H); see also Table 3. − $C_{11}H_{13}N_3O_3$ (235.2): calcd. C 56.16, H 5.57, N 17.85; found C 56.01, H 5.19, N 17.44. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.35 (m, 5 H), 5.10 (d, 1 H, *J* = 1.6 Hz), 5.09 (s, 1 H), 4.53 and 4.75 (ABdd, 2 H, *J* = 12.2 Hz), 4.32 (dd, 1 H, *J* = 8.8 and 7.2 Hz), 3.96 (ddd, 1 H, *J* = 6.0 and 1.5 Hz), 3.83 (dd, 1 H, *J* = 9.1 and 5.9 Hz), 2.09 (s, 3 H). − $C_{13}H_{15}N_3O_4$ (277.3): calcd. C 56.31, H 5.45, N 15.14; found C 56.09, H 5.37, N 15.45.

Azidolysis of Epoxides **1−4** *with NaN_3/$LiClO_4$ in MeCN − General Procedure:* A solution of the epoxide (0.50 mmol) in anhydrous MeCN (2.0 ml) was treated with NaN_3 (0.040 g, 0.61 mmol) and $LiClO_4$ (0.53 g, 5.0 mmol) and the reaction mixture was stirred at 80°C for 18 h. Standard work-up afforded a crude product, which was analyzed by GC and ^{1}H-NMR spectroscopy, giving the results shown in Tables 1 and 2.

Aminolysis of Epoxides **1−4** *with $NHEt_2$/EtOH:* The following procedure is typical. A solution of the epoxide *cis* **1** (0.095 g, 0.50 mmol) in anhydrous EtOH (0.6 ml) was treated with $NHEt_2$ (0.091 g, 1.25 mmol) and the reaction mixture was stirred at 80°C for 3 days. Dilution with diethyl ether and concentration of the washed (saturated aqueous NaCl) organic solution afforded a crude reaction product (0.123 g) consisting of an 87:13 mixture of amino alcohols **25** and **26** (GC), which was subjected to preparative TLC using a 3:1:1 mixture of hexane, $CHCl_3$, and NEt_3 as eluent. Extraction of the two most intense bands afforded pure amino alcohols **25** (0.082 g) and **26** (0.011 g).

rel-(1R,2S,5S)-2-(Benzyloxy)-5-(N,N-diethylamino)-1-cyclopentanol (**25**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.22−7.35 (m, 5 H), 4.53 and 4.60 (ABdd, 2 H, *J* = 11.8 Hz), 3.94 (t, 1 H, *J* = 5.6 Hz), 3.83 (dd, 1 H, *J* = 5.6 Hz), 3.01 (ddd, 1 H, *J* = 8.3 and 5.6 Hz), 2.68 (q, 4 H, *J* = 7.1 Hz), 1.81−2.01 (m, 2 H), 1.63−1.79 (m, 1 H), 1.34−1.50 (m, 1 H), 1.03 (t, 6 H, *J* = 7.1 Hz); see also Table 3. − $C_{16}H_{25}NO_2$ (263.4): calcd. C 72.96, H 9.56, N 5.31; found C 73.09, H 9.87, N 5.20. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.22−7.36 (m, 5 H), 5.15 (t, 1 H, *J* = 5.8 Hz), 4.49 (s, 2 H), 3.95 (q, 1 H, *J* = 5.7 Hz), 3.40 (td, 1 H, *J* = 8.0 and 6.5 Hz), 2.62 (q, 4 H, *J* = 7.1 Hz), 2.08 (s, 3 H), 1.66−2.04 (m, 3 H), 1.40−1.58 (m, 1 H), 1.04 (t, 6 H, *J* = 7.1 Hz). − $C_{18}H_{27}NO_3$ (305.4): calcd. C 70.78, H 8.91, N 4.58; found C 70.49, H 9.10, N 4.91.

rel-(1R,2S,3S)-3-(Benzyloxy)-2-(N,N-diethylamino)-1-cyclopentanol (**26**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.34 (m, 5 H), 4.42 and 4.55 (ABdd, 2 H, *J* = 11.8 Hz), 3.87−3.97 (m, 2 H), 3.04 (dd, 1 H, *J* = 7.1 and 6.0 Hz), 2.55−2.74 (m, 4 H), 1.71−1.90 (m, 4 H), 1.08 (t, 6 H, *J* = 7.1 Hz); see also Table 3. − $C_{16}H_{25}NO_2$ (263.4): calcd. C 72.96, H 9.56, N 5.31; found C 72.98, H 9.40, N 5.42.

The crude reaction product (0.115 g) from the epoxide *trans* **2** was found to consist of essentially pure *rel-(1R,2R,5S)-2-(benzyloxy)-5-(N,N-diethylamino)-1-cyclopentanol* (**41**) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.38 (m, 5 H), 4.59 and 4.60 (ABdd, 2 H, *J* = 11.7 Hz), 3.92 (dd, 1 H, *J* = 8.3 and 5.7 Hz), 3.74−3.80 (m, 1 H), 2.90−2.99 (m, 1 H), 2.45−2.86 (m, 2 H), 1.91−1.96 (m, 1 H), 1.62−1.73 (m, 3 H), 1.04 (t, 6 H, *J* = 7.1 Hz); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 139.2, 129.0, 128.4, 128.1, 83.8, 79.4, 71.8, 67.4, 44.6, 27.6, 21.7, 14.0. − $C_{16}H_{25}NO_2$ (263.4): C 72.96, H 9.56, N 5.31; found C 72.65, H 9.38, N 5.54.

The crude reaction product (0.124 g) from the epoxide *cis* **3**, consisting of an 85:15 mixture (GC) of amino alcohols **33** and **34**, was subjected to preparative TLC using a 3:1:1 mixture of hexane, $CHCl_3$, and NEt_3 as eluent. Extraction of the two most intense bands (the faster moving band contained **33**) afforded pure amino alcohols **33** (0.078 g) and **34** (0.013 g).

D,L-Benzyl-3-deoxy-3-(β-N,N-diethylamino)-α-erythrofuranoside (**33**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.41 (m, 5 H), 5.05 (d, 1 H, *J* = 4.7 Hz), 4.55 and 4.81 (ABdd, 2 H, *J* = 11.7 Hz), 4.08−4.17 (m, 2 H), 3.77 (dd, 1 H, *J* = 9.1 and 6.2 Hz), 3.31 (dd, 1 H, *J* = 14.4 and 6.6 Hz), 2.53−2.80 (m, 4 H), 1.04 (t, 6 H, *J* = 7.1 Hz); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 137.9, 129.1, 128.7, 128.6, 101.6, 75.8, 70.1, 69.7, 66.4, 44.6, 12.3. − $C_{15}H_{23}NO_3$ (265.4): calcd. C 67.89, H 8.73, N 5.27; found C 67.61, H 8.49, N 5.34.

D,L-Benzyl-2-deoxy-2-(β-N,N-diethylamino)-α-erythrofuranoside (**34**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.35 (m, 5 H), 5.07 (d, 1 H, *J* = 1.5 Hz), 4.48 and 4.76 (ABdd, 2 H, *J* = 11.8 Hz), 4.28 (ddd, 1 H, *J* = 6.4 and 4.0 Hz), 4.15 (dd, 1 H, *J* = 9.1 and 6.7 Hz), 3.83 (dd, 1 H, *J* = 9.1 and 6.3 Hz), 3.26 (dd, 1 H, *J* = 3.8 and 1.6 Hz), 2.47−2.69 (m, 4 H), 1.05 (t, 6 H, *J* = 7.1 Hz); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.2, 129.0, 128.5, 128.3, 104.3, 75.7, 73.9, 73.1, 69.7, 45.1, 12.9. − $C_{15}H_{23}NO_3$ (265.4): C 67.89, H 8.73, N 5.27; found C 67.71, H 8.95, N 5.01.

The crude reaction product (0.119 g) from the epoxide *trans* **4** was found to consist of essentially pure *D,L-benzyl-3-deoxy-3-(β-N,N-diethylamino)-β-erythrofuranoside* (**45**) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.20−7.41 (m, 5 H),

4.96 (d, 1 H, J = 1.1 Hz), 4.46 and 4.73 (ABdd, 2 H, J = 11.8 Hz), 4.19 (dd, 1 H, J = 4.5 and 1.0 Hz), 4.08 (t, 1 H, J = 8.4 Hz), 2.82 (t, 1 H, J = 8.7 Hz), 3.26 (ddd, 1 H, J = 12.3, 8.2 and 4.6 Hz), 2.62 (q, 4 H, J = 7.2 Hz), 1.02 (t, 6 H, J = 7.1 Hz); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.3, 129.0, 128.6, 128.3, 108.9, 80.1, 70.4, 69.4, 68.5, 45.0, 12.53. − $C_{15}H_{23}NO_3$ (265.4): calcd. C 67.89, H 8.73, N 5.27; found C 67.70, H 9.04, N 5.57.

Aminolysis of Epoxides **1**−**4** *with $NHEt_2$/$LiClO_4$ in MeCN − General Procedure:* A solution of the epoxide (0.37 mmol) in anhydrous MeCN (1.5 ml) was treated with $NHEt_2$ (0.38 ml, 3.7 mmol) and $LiClO_4$ (0.795 g, 7.5 mmol) and the reaction mixture was stirred at 80°C for 18 h. Standard work-up afforded a crude reaction product, which was analyzed by GC and ^{1}H-NMR spectroscopy, giving the results shown in Tables 1 and 2.

Ring-Opening of Epoxides **1**−**4** *with PhSH/NEt_3:* The following procedure is typical. A solution of the epoxide *cis* **1** (0.095 g, 0.50 mmol) in MeOH (0.5 ml) was treated with PhSH (0.17 g, 1.5 mmol) and NEt_3 (0.202 g, 2.0 mmol) and the reaction mixture was stirred at room temperature for 18 h. Dilution with diethyl ether and concentration of the washed (saturated aqueous $NaHCO_3$ and NaCl) organic solution afforded a crude product (0.142 g) consisting of an 80:20 (^{1}H NMR) mixture of hydroxy thioethers **27** and **28**, which was subjected to preparative TLC using a 9:1 mixture of petroleum ether and AcOEt as eluent. Extraction of the two most intense bands (the faster moving band contained **27**) afforded pure hydroxy thioethers **27** (0.080 g) and **28** (0.020 g).

rel-(1*R*,2*R*,5*R*)-*2-(Benzyloxy)-5-(phenylthio)-1-cyclopentanol* (**27**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.16−7.42 (m, 10 H), 4.53 and 4.58 (ABdd, 2 H, J = 11.6 Hz), 3.97−4.10 (m, 2 H), 3.53−3.62 (m, 1 H), 2.27−2.45 (m, 1 H), 1.92−2.06 (m, 1 H), 1.74−1.88 (m, 1 H), 1.49−1.62 (m, 1 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.3, 136.3, 130.7, 129.5, 129.2, 128.6, 128.4, 127.0, 80.4, 72.4, 50.7, 28.5, 28.3. − $C_{18}H_{20}O_2S$ (300.4): calcd. C 71.96, H, 6.71; found C 71.72, H 7.01.

rel-(1*R*,2*S*,3*S*)-*3-(Benzyloxy)-2-(phenylthio)-1-cyclopentanol* (**28**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.17−7.51 (m, 10 H), 4.47 (s, 2 H), 4.02−4.15 (m, 1 H), 3.88−3.92 (m, 1 H), 3.59 (t, 1 H, J = 3.0 Hz), 1.59−2.10 (m, 4 H); see also Table 3. − $C_{18}H_{20}O_2S$ (300.4): C 71.96, H 6.71; found C 72.15, H 6.98.

The crude reaction product (0.138 g) from the epoxide *trans* **2** was subjected to preparative TLC using an 8:2 mixture of petroleum ether and diethyl ether as eluent. Extraction of the most intense band afforded pure *rel*-(1*R*,2*S*,5*R*)-*2-(benzyloxy)-5-(phenylthio)-1-cyclopentanol* (**42**) as a liquid (0.095 g). − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.41−7.46 (m, 2 H), 7.18−7.40 (m, 8 H), 4.57 (s, 2 H), 3.97 (dd, 1 H, J = 7.7 and 5.7 Hz), 3.78−3.87 (m, 1 H), 3.26 (q, 1 H, J = 8.0 Hz), 1.92−2.36 (m, 2 H), 1.66−1.87 (m, 2 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.9, 135.1, 132.4, 129.6, 129.0, 128.4, 128.3, 127.7, 84.9, 83.0, 72.2, 52.2, 29.1, 28.5. − $C_{18}H_{20}O_2S$ (300.4): calcd. C 71.96, H 6.71; found C 71.84, H 6.88.

The crude reaction product (0.144 g) from the epoxide *cis* **3**, consisting of an 80:20 mixture of hydroxy thioethers **35** and **36** (GC), was subjected to preparative TLC using a 9:1 mixture of petroleum ether and AcOEt as eluent. Extraction of the two most intense bands (the faster moving band contained **35**) afforded pure hydroxy thioethers **35** (0.086 g) and **36** (0.021 g).

D,L-Benzyl-3-deoxy-3-(β-phenylthio)-α-erythrofuranoside (**35**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.23−7.46 (m, 10 H), 5.13 (d, 1 H, J = 4.5 Hz), 4.58 and 4.83 (ABdd, 2 H, J = 11.7 Hz), 4.38 (dd, 1 H, J = 9.1 and 7.9 Hz), 4.05−4.18 (m, 1 H), 3.82 (dd, 1 H, J = 9.3 and 6.2 Hz), 3.64 (dd, 1 H, J = 13.6 and 6.6 Hz); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 137.6, 134.7, 132.0, 129.7, 129.2, 128.7, 127.8, 101.0, 77.8, 71.7, 70.3, 51.2. − $C_{17}H_{18}O_3S$ (302.4): calcd. C 67.52, H 5.99; found C 67.70, H 6.25.

D,L-Benzyl-2-deoxy-2-(β-phenylthio)-α-erythrofuranoside (**36**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.19−7.40 (m, 10 H), 5.16 (s, 1 H), 4.50 and 4.77 (ABdd, 2 H, J = 11.7 Hz), 4.38 (dd, 1 H, J = 9.7 and 5.0 Hz), 4.16−4.25 (m, 1 H), 4.03 (dd, 1 H, J = 9.8 and 1.9 Hz), 3.75 (s, 1 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 137.6, 134.4, 131.1, 129.9, 129.2, 128.6, 127.8, 106.8, 76.5, 76.2, 70.1, 57.9. − $C_{17}H_{18}O_3S$ (302.4): C 67.52, H 5.99; found C 67.46, H 5.67.

The crude reaction product (0.143 g) from the *trans* epoxide **4** was found to consist of essentially pure *D,L-benzyl-3-deoxy-3-(β-phenylthio)-β-erythrofuranoside* (**46**) as a solid, m.p. 63−64°C. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.16−7.41 (m, 10 H), 5.03 (s, 1 H), 4.46 and 4.73 (ABdd, 2 H, J = 11.9 Hz), 4.37 (t, 1 H, J = 8.4 Hz), 4.20−4.29 (m, 1 H), 3.86 (t, 1 H, J = 8.6 Hz), 3.55 (ddd, 1 H, J = 8.0 and 4.0 Hz); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.7, 136.0, 131.5, 130.1, 129.3, 128.8, 128.7, 127.9, 108.7, 83.3, 72.8, 69.9, 52.6. − $C_{17}H_{18}O_3S$ (302.4): C 67.52, H 5.99; found C 67.88, H 6.34.

Ring-Opening of Epoxides **1**−**4** *with PhSH/$LiClO_4$ in MeCN − General Procedure:* A solution of the epoxide (0.3 mmol) in anhydrous MeCN (0.6 ml) was treated with PhSH (0.048 ml, 0.45 mmol) and $LiClO_4$ (0.16 g, 1.5 mmol) and the reaction mixture was stirred at 80°C for 18 h. Standard work-up afforded a crude reaction product, which was analyzed by ^{1}H-NMR spectroscopy, giving the results shown in Tables 1 and 2.

Reaction of Epoxides **1**−**4** *with $LiAlH_4$:* The following procedure is typical. A solution of epoxide *cis* **1** (0.114 g, 0.60 mmol) in anhydrous pentane (4.0 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (0.15 g) in anhydrous pentane (10 ml) and the mixture was stirred at room temperature for 2 h. Standard work-up afforded a crude reaction product (0.11 g) consisting of a 55:45 mixture (GC) of alcohols **29** and **30**, which was subjected to preparative TLC using a 9:1 mixture of petroleum ether and AcOEt as eluent. Extraction of the two most intense bands (the faster moving band contained **29**) afforded pure alcohols **29** (0.050 g) and **30** (0.038 g).

rel-(1*R*,2*S*)-*2-(Benzyloxy)-1-cyclopentanol* (**29**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.36 (m, 5 H), 4.50 and 4.58 (ABdd, 2 H, J = 11.7 Hz), 4.02−4.15 (m, 1 H), 3.81 (ddd, 1 H, J = 6.4 and 4.3 Hz), 1.66−1.87 (m, 5 H), 1.43−1.57 (m, 1 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.8, 129.1, 128.4, 128.3, 82.0, 72.8, 72.1, 31.7, 28.5, 20.3. − $C_{12}H_{16}O_2$ (192.3): calcd. C 74.96, H 8.32; found C 74.71, H 8.20. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.34 (m, 5 H), 5.14−5.20 (m, 1 H), 4.52 and 4.60 (ABdd, 2 H, J = 11.9 Hz), 3.86 (ddd, 1 H, J = 6.9 and 4.2 Hz), 2.09 (s, 3 H), 1.74−2.00 (m, 5 H), 1.50−1.70 (m, 1 H). − $C_{14}H_{18}O_3$ (234.3): C 71.76, H 7.74; found C 71.49, H 8.05.

rel-(1*R*,3*S*)-*3-(Benzyloxy)-1-cyclopentanol* (**30**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.22−7.34 (m, 5 H), 4.49 (s, 2 H), 4.18−4.35 (m, 1 H), 4.09 (ddd, 1 H, J = 5.0 and 2.2 Hz), 1.69−2.16 (m, 6 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 138.9, 129.0, 128.2, 81.2, 74.0, 71.3, 42.0, 34.6, 30.7. − $C_{12}H_{16}O_2$ (192.3): calcd. C 74.96, H 8.32; found C 78.24, H 8.05. *Acetate:* Liquid. − ^{1}H NMR ($CDCl_3$): δ = 7.25−7.40 (m, 5 H), 5.05−5.11 (m, 1 H), 4.49 (s, 2 H), 3.96−4.01 (m, 1 H), 2.20−2.35 (m, 1 H), 2.03 (s, 3 H), 1.77−1.95 (m, 5 H). − $C_{14}H_{18}O_3$ (234.3): calcd. C 71.76, H 7.74; found C 71.97, H 7.91.

The crude reaction product (0.11 g) obtained from the epoxide *trans* **2** was found to consist of essentially pure *rel*-(1*R*,2*R*)-*2-(benzyloxy)-1-cyclopentanol* (**43**) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.35 (m, 5 H), 4.51 and 4.57 (ABdd, 2 H, *J* = 11.8 Hz), 4.11−4.21 (m, 1 H), 3.72−3.80 (m, 1 H), 1.91−2.08 (m, 2 H), 1.45−1.79 (m, 4 H); see also Table 3. − ^{13}C NMR ($CDCl_3$): δ = 139.2, 129.1, 128.3, 128.2, 87.2, 78.1, 72.1, 32.7, 30.0, 21.1. − $C_{12}H_{16}O_2$ (192.3): calcd. C 74.96, H 8.32; found C 74.81, H 8.10.

The crude reaction product (0.11 g) from the epoxide *cis* **3**, consisting of a 35:65 mixture of the two alcohols **37** and **38**, was subjected to preparative TLC using a 9:1 mixture of petroleum ether and AcOEt as eluent. Extraction of the two most intense bands (the faster moving band contained **37**) afforded pure alcohols **37** (0.031 g) and **38** (0.058 g).

D,L-Benzyl-3-deoxy-α-erythrofuranoside (**37**): Liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.38 (m, 5 H), 5.02 (d, 1 H, *J* = 4.4 Hz), 4.58 and 4.84 (ABdd, 2 H, *J* = 11.8 Hz), 4.15−4.35 (m, 1 H), 4.06 (ddd, 1 H, *J* = 8.6 and 5.2 Hz), 3.87 (q, 1 H, *J* = 7.5 Hz), 2.14−2.30 (m, 1 H), 1.80−1.98 (m, 1 H); see also Table 3. − $C_{11}H_{14}O_3$ (194.2): calcd. C 68.02, H 7.26; found C 68.14, H 7.35.

D,L-Benzyl-2-deoxy-α-erythrofuranoside (**38**): Liquid: IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.26−7.37 (m, 5 H), 5.27 (d, 1 H, *J* = 4.3 Hz), 4.50 and 4.78 (ABdd, 2 H, *J* = 11.8 Hz), 4.27−4.42 (m, 1 H), 4.06 (m, 2 H), 1.96−2.19 (m, 2 H); see also Table 3. − $C_{11}H_{14}O_3$ (194.2): C 68.02, H 7.26; found C 68.37, H 7.59.

The crude reaction product (0.11 g) from the epoxide *trans* **4** was found to consist of *D,L-benzyl-3-deoxy-β-erythrofuranoside* (**47**) as a liquid. − IR (CCl_4), see Table 3. − ^{1}H NMR ($CDCl_3$): δ = 7.18−7.30 (m, 5 H), 4.92 (s, 1 H), 4.39 and 4.63 (ABdd, 2 H, *J* = 11.7 Hz), 4.21 (dd, 1 H, *J* = 5.6 and 1.3 Hz), 4.05 (dd, 1 H, *J* = 15.9 and 8.0 Hz), 3.92 (ddd, 1 H, *J* = 13.6, 9.1 and 4.6 Hz), 2.14−2.32 (m, 1 H), 1.69−1.82 (m, 1 H); see also Table 3. − $C_{11}H_{14}O_3$ (194.2): calcd. C 68.02, H 7.26; found C 67.88, H 7.01.

Reaction of cis Epoxides **1** *and* **3** *with $LiAlH_4$ in the Presence of 12-Crown-4:* The following procedure is typical. A suspension of $LiAlH_4$ (0.040 g, 1.0 mmol) in anhydrous pentane (6 ml) was treated with 12-crown-4 (0.194 g, 1.1 mmol) and the mixture was stirred at room temperature for 15 h. Epoxide **1** (0.057 g, 0.3 mmol) in anhydrous pentane (2 ml) was then added and the mixture was stirred at room temperature for 18 h. Standard work-up afforded a crude reaction product, which was analyzed by GC and ^{1}H-NMR spectroscopy, giving the results shown in Table 1.

[1] [1a] E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker, L. Deng, *J. Am. Chem. Soc.* **1991**, *113*, 7063−7064, and references therein. − [1b] T. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.* **1980**, *102*, 5974−5976.

[2] [2a] J. Gorzynski Smith, *Synthesis* **1984**, 629−656. − [2b] R. E. Parker, N. S. Isaacs, *Chem. Rev.* **1959**, *59*, 737−799.

[3] [3a] P. Crotti, V. Di Bussolo, L. Favero, N. Jannitti, M. Pineschi, M. Pasero, *Gazz. Chim. Ital.* **1997**, 127, 79−90. − [3b] F. Calvani, P. Crotti, C. Gardelli, M. Pineschi, *Tetrahedron* **1994**, *50*, 12999−13021. − [3c] M. Chini, P. Crotti, C. Gardelli, F. Macchia, *J. Org. Chem.* **1994**, *59*, 4131−4137. − [3d] M. Chini, P. Crotti, C. Gardelli, F. Macchia, *Tetrahedron* **1994**, *50*, 1261−1274. − [3e] M. Chini, P. Crotti, L. A. Flippin, C. Gardelli, E. Giovani, F. Macchia, M. Pineschi, *J. Org. Chem.* **1993**, *58*, 1221−1227. − [3f] M. Chini, P. Crotti, L. A. Flippin, F. Macchia, *J. Org. Chem.* **1990**, *55*, 4265−4272. − [3g] M. Chini, P. Crotti, L. A. Flippin, F. Macchia, *Tetrahedron Lett.* **1989**, *30*, 6563−6566. − [3h] L. A. Flippin, P. A. Brown, K. Jalali-Araghi, *J. Org. Chem.* **1989**, *54*, 3588−3596. − [3i] M. Caron, P. R. Carlier, K. B. Sharpless, *J. Org. Chem.* **1988**, *53*, 5185−5187. − [3j] M. Caron, K. B. Sharpless, *J. Org. Chem.* **1985**, *50*, 1557−1560. − [3k] J. M. Chong, K. B. Sharpless, *J. Org. Chem.* **1985**, *50*, 1560−1563. − [3l] C. H. Behrens, K. B. Sharpless, *J. Org. Chem.* **1985**, *50*, 5696−5704.

[4] M. Colombini, P. Crotti, V. Di Bussolo, L. Favero, C. Gardelli, F. Macchia, M. Pineschi, *Tetrahedron* **1995**, *51*, 8089−8112.

[5] K. E. Wilson, R. T. Seidner, S. Masamune, *J. Chem. Soc., Chem. Commun.* **1970**, 213−214.

[6] [6a] I. B. Campbell, E. W. Collington, H. Finch, P. Hallett, R. Hayes, P. Lumley, K. Mills, C. J. Wallis, B. P. White, *Bioorg. Med. Chem. Lett.* **1991**, *1*, 689−694. − [6b] T. Itoh, K. Jitsukowa, K. Kaneda, S. Terarishi, *J. Am. Chem. Soc.* **1979**, *101*, 159−169. − [6c] R. Steyn, H. Z. Sable, *Tetrahedron* **1969**, *25*, 3579−3597. − [6d] A. H. Hoveyda, D. A. Evans, G. C. Fu, *Chem. Rev.* **1993**, *93*, 1307−1370, and references therein.

[7] All the structures depicted in the formulas and in Schemes 1−6 represent one enantiomeric series of the racemic mixtures used in this study.

[8] A. P. Kozikowski, K. L. Sorgi, R. J. Schmiesing, *J. Chem. Soc., Chem. Commun.* **1980**, 477−479.

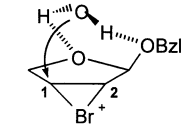
[9] H. J. Reich, *Acc. Chem. Res.* **1979**, *12*, 22−30.

[10] C. H. Gagnieu, A. U. Grouiller, *J. Chem. Soc., Perkin Trans. 1* **1982**, 1009−1011.

[11] The result obtained with PBIA is in agreement with a preferential attack of the electrophile on the face of olefin **18** opposite to the OBzl substituent, as observed in the case of **8**.

[12] Due to their instability, the bromohydrins (presumably **19** and **20**) formed in the reaction of olefin **18** with NBS in THF/H_2O (Scheme 3) were not separated, but were directly cyclized (aqueous 1 N NaOH) to the corresponding mixture of epoxides **3** and **4**. The consistent *syn* selectivity observed in the NBS,THF-H_2O/NaOH protocol on olefin **18** points to a preferential reactivity of the intermediate bromonium ion **62** as a consequence of a favorable interaction (hydrogen bond) of the nucleophile (H_2O) with both the exocyclic and the endocyclic oxygens of the acetal functionality, as tentatively shown (see below).

62



[13] The classic $LiAlH_4$ reduction should be regarded as being carried out under chelating conditions, due to the presence of the Li^+ cation of the reagent. The same reaction carried out in the presence of a crown ether (12-crown-4) should however be considered as operating under non-chelating conditions, due to the sequestering ability of the crown ether specific for Li^+.

[14] Epoxide **3** appears to be more sensitive than **1** to the opening chelating conditions. This could be due to the presence of the two oxygens of the acetal functionality which increase the chelating ability of **3** with respect to **1**, where only one oxygen (the exocyclic ether oxygen) is present.

[15] The behaviour of the cyclopentane- and 2,5-dihydrofuran-derived epoxides **1** and **3** (this work) is similar to the one observed with the corresponding cyclohexane- and 5,6-dihydro-2*H*-pyran-derived epoxides, previously studied.[3b]

[16] [16a] M. Tichy, in *Advances in Organic Chemistry, Methods and Results* (Eds.: R. A. Raphael, E. C. Taylor, H. Winberg), Interscience, New York, **1965**, Vol. 5, p. 115−298. − [16b] B. Macchia, F. Macchia, L. Monti, *Gazz. Chim. Ital.* **1970**, *100*, 35−63.

[17] R. Steyn, H. Z. Sable, *Tetrahedron* **1971**, *27*, 4429−4447.

[18] For epoxides **3** and **4**, the appearance in their ^{1}H-NMR spectra of the signal of proton H_3 as a singlet prevents a similar conformational analysis as performed above for **1** and **2**. Epoxides **3** and **4** were analyzed by means of the PC-MODEL program,[3b][19] which found for their minimum energy conformations an $H_3-C(3)-C(2)-H_2$ dihedral angle of +49° in **3** and of −74° in **4**. This indicates that both epoxides preferentially adopt the corresponding boat conformation **a** (Scheme 5).[17]

[19] *PC-MODEL, ver. 4.0*; Serena Software, Bloomington, Indiana, USA, **1990**.

[20] The presence of only one band attributable to a free OH group in the IR spectra (CCl_4) of both the *C-1 products* (bromohydrin **12** and compounds **39**−**47**, Scheme 4) and the *C-2 products* (only bromohydrin **9**; compounds **48**−**56** were not obtained, Scheme 4)[21] from *trans* epoxides **2** and **4**, respectively, makes

IR analysis of these compounds insufficient to distinguish between the two *trans* regioisomers that can theoretically be obtained in the ring-opening reactions of these epoxides. However, by accurate examination of the ^{1}H-NMR spectra, with appropriate double resonance experiments, the *C-1 product* regiochemistry can be unequivocally assigned to bromohydrin **12** and compounds **39**−**47**, while the *C-2 product* regiochemistry can be assigned to bromohydrin **9**, as shown in Scheme 4.

[21] *C-2 products* were not obtained from the epoxide *trans* **4** (Scheme 4). However, from examination of appropriate molecular models (Scheme 6) the IR spectra of these compounds in dilute CCl_4 solution can be expected to be quite similar (presence of only a free OH) to those of the obtained regioisomeric *C-1 products* (see text and Table 3).

[98171]