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Regiochemical Control of the Ring Opening of 1,2-Epoxides by Means of Chelating Processes. 8. Synthesis and Ring Opening Reactions of cis- and trans-Oxides Derived from 3-Benzyloxycyclohexene and 2-Benzyloxy-5,6-dihydro-2*H*-pyran[1]

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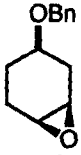
Dedicated to Prof. G.Berti on the occasion of his 70th birthday

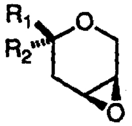
Abstract : The regiochemical outcome of the ring opening of 1,2-epoxides bearing polar remote functionalization through chelation processes assisted by metal ions, was verified in cyclic oxirane systems having the polar functionality in an allylic position to the oxirane ring. The diastereoisomeric cis/trans epoxide pairs **5**,**6** and **7**,**8** derived from 3-benzyloxycyclohexene, and 2-benzyloxy-5,6-dihydro-2*H*-pyran, respectively, were prepared and several of their opening reactions were studied. The regioselectivity observed largely depends on the reaction conditions (standard or metal-assisted) and, interestingly, on the nature of the nucleophile used.

1,2-Epoxides constitute one of the most important functional groups in organic chemistry: their easy availability and their ability to react with a large variety of nucleophiles (C, O, and N-nucleophiles, halogenide, hydride, etc) make 1,2-epoxides a valuable tool in organic synthesis for the construction of two adjacent stereocenters, once the regiochemistry of the opening process can be effectively driven.[2] In fact, whereas the opening process of typically aliphatic and cycloaliphatic 1,2-epoxides is completely anti stereoselective,[3] the regiochemistry observed in non-symmetrical systems can unfortunately be highly random. As a consequence, large efforts have been made in the last few years in order to devise reaction conditions and new methodologies able to carry out the opening process of 1,2-epoxides with nucleophiles under a rigid stereocontrol.

Our previous results in this field had shown that the presence of a protected heterofunctionality (OBn) in a homoallylic or homologous position with respect to the oxirane ring, in a cycloaliphatic system, was able to modify the regiochemical outcome of the opening process, depending on the operating conditions.[1,4] The best results were obtained with the cis epoxide **1**, in which the OBn functionality is directly linked to the cyclohexane ring in a homoallylic relation to the oxirane system.[4] In the reaction of **1** with nucleophiles, the regioselectivity turned out to be closely linked to the type of catalysis and to the presence of metallic species in the reaction medium to the point that a nice regioalternating process was found, which was attributed to the incursion of chelated species of type **69** (Scheme 3).[4] We also found that a polar group inserted into a cyclic system, as in the tetrahydropyranil epoxide **2**, can effectively intervene in directing the epoxide ring opening by means of chelating processes assisted by metal ions.[5] These studies are now extended to the



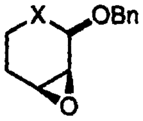
1



2, R_1=R_2=H

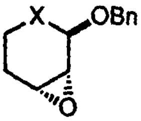
3, R_1=OBn; R_2=H

4, R_1=H; R_2=OBn



5
7

X=CH_2
X=O



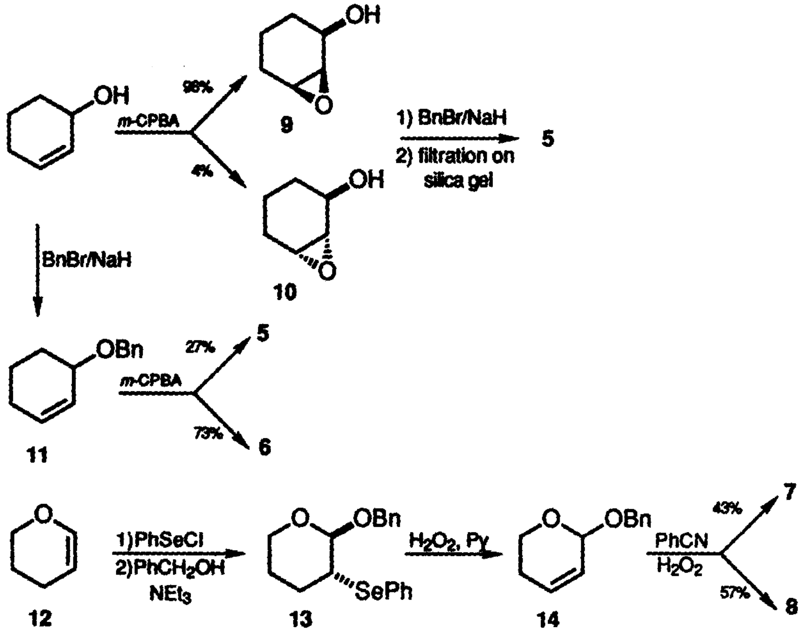
6
8

diastereoisomeric epoxides cis **5** and trans **6**: it appeared to be particularly interesting to evaluate whether the allylic OBn functionality of these 1,2-epoxycyclohexanes is able, at least in the cis diastereoisomer **5**, to effectively influence the regiochemical results of the oxirane ring opening process, as it is in the isomeric structurally related cis epoxides **1** and **3**.[1,4] As a consequence, the cis **5** and the trans epoxide **6** were synthesized and some their opening reactions were examined. In an attempt to examine oxirane systems more closely related to naturally occurring compounds and particularly to deoxysugars,[1,5] also the benzyloxy tetrahydropyranyl epoxides cis **7** and trans **8**, structurally related both to **5** and **6**, and to the previously studied epoxides **3** and **4**,[1] respectively, were synthesized and some of their opening reactions were studied.

Results

Following Ganem's procedure,[6] the reaction of 2-cyclohexen-1-ol with *m*-CPBA afforded a 96:4 mixture of epoxy alcohols cis **9** and trans **10** which were alkylated with BnBr/NaH system to give a corresponding mixture of epoxides cis **5** and trans **6**. Simple filtration of this mixture through a silica gel column afforded pure cis epoxide **5**. On the other hand, *m*-CPBA oxidation of the olefin **11** afforded a 27:73 mixture of epoxides cis **5** and trans **6** which were separated by flash-chromatography (Scheme 1). Reaction of benzenselenyl chloride with 3,4-dihydro-2*H*-pyran (**12**), followed by treatment with benzyl alcohol in the presence of triethylamine afforded the known phenylselenyl acetal **13**.[7] Treatment of a solution of **13** in CH_2Cl_2/Py with 36% H_2O_2[8] yielded, after filtration on silica gel column, pure olefin **14**. Oxidation of **14** with peroxybenzimidic acid[9] afforded a 43:57 mixture of epoxides cis **7** and trans **8** which were separated by flash-chromatography. A slightly different diastereoselectivity was observed in the *m*-CPBA oxidation of **14** and in the base-promoted cyclization of the mixture of bromohydrins obtained in the reaction of **14** with N-bromosuccinimide (NBS) in an aqueous solvent (**7**:**8** ratio=25:75 and 37:63, respectively).

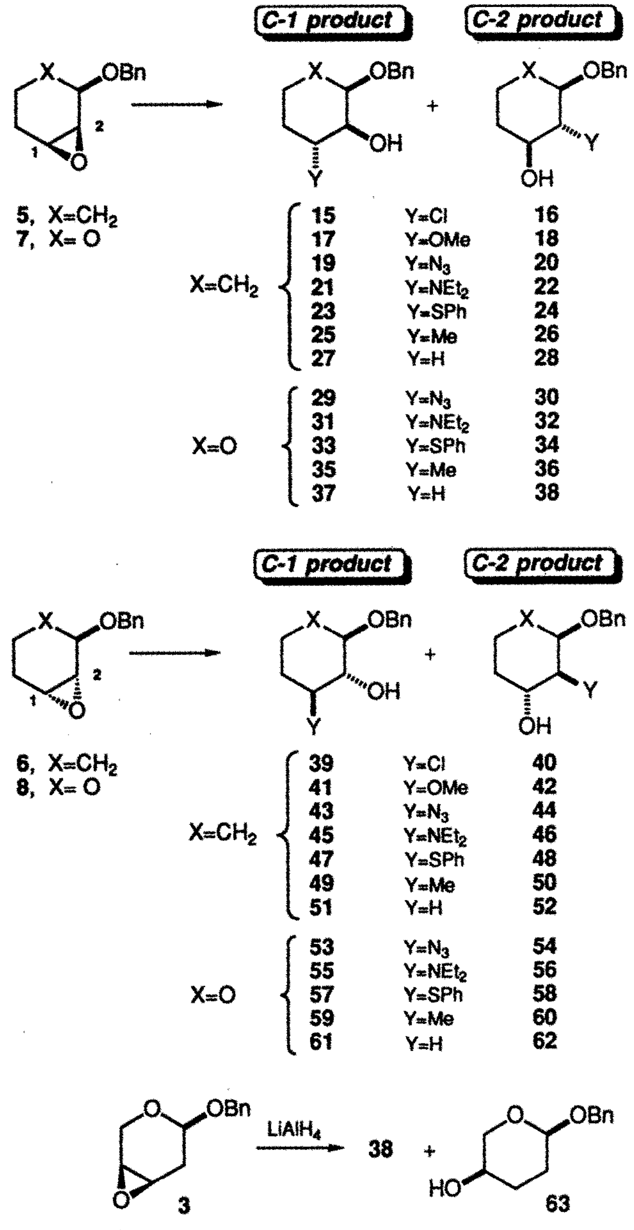
SCHEME 1



The cis epoxides **5** and **7**, and the trans epoxides **6** and **8** were subjected to several ring-opening reactions with different nucleophiles (Scheme 2) both under standard non-chelating conditions (reactions carried out under classic acidic proton catalysis or without any catalysis) and under conditions which had proved to be useful in other systems in order to get evidence of the incursion of chelate species (reactions carried out in the presence of a metal salt or a metallic species). The results obtained are shown in Tables 1 and 2. The determination of the relative amounts of the regioisomeric addition products (*C-1* and *C-2 products*)^{10} in the opening reactions of epoxides **5-8** was accomplished by GC analysis of the crude reaction mixture and/or by GC and ^{1}H NMR analysis of the acetylated crude reaction product.

Under standard non-chelating conditions, with the only exception of the reaction with Me_2CuLi, $AlMe_3$ and $LiAlH_4$ (vide infra),^{4c,d} the ring opening process of cis epoxide **5** proceeds with the attack of the nucleophile (Cl^-, MeOH, N_3^-, $NHEt_2$, PhSH) on the C-(1) oxirane carbon to give *C-1 products*, almost exclusively, no trace of regioisomeric *C-2 products* being detected. When the same reactions of **5** were carried out under chelating conditions, that is in the presence of a metal ion in a non-protic solvent, such as CH_3CN, the regioselectivity of the opening process changes, even substantially in some cases, and, with the only exception of the addition reaction of Cl^- and MeOH, different amounts of the regioisomeric *C-2 products* are also formed (see Table 1). The reactions of **5** with Me_2CuLi, $AlMe_3$ and $LiAlH_4$ carried out under usual standard conditions reveal a different behavior. In these conditions, mixtures of *C-1* and *C-2 products* are formed in which, however, the former still prevail (68-99%, entries 15, 16 and 18, Table 1).

SCHEME 2



X	C-1 product	Y	C-2 product
X=CH$_2$	15	Y=Cl	16
	17	Y=OMe	18
	19	Y=N$_3$	20
	21	Y=NEt$_2$	22
	23	Y=SPh	24
	25	Y=Me	26
	27	Y=H	28
X=O	29	Y=N$_3$	30
	31	Y=NEt$_2$	32
	33	Y=SPh	34
	35	Y=Me	36
	37	Y=H	38

X	C-1 product	Y	C-2 product
X=CH$_2$	39	Y=Cl	40
	41	Y=OMe	42
	43	Y=N$_3$	44
	45	Y=NEt$_2$	46
	47	Y=SPh	48
	49	Y=Me	50
	51	Y=H	52
X=O	53	Y=N$_3$	54
	55	Y=NEt$_2$	56
	57	Y=SPh	58
	59	Y=Me	60
	61	Y=H	62

Table 1. Regioselectivity of the Ring Opening Reactions of the cis Epoxides 5 and 7 Under Non-Chelating and Chelating Conditions.

entry	epoxide	reagents	solvent	reaction time and temperature	*C-1 product*		*C-2 product*		yield %
1	**5**	HCl	$CHCl_3$	10 min (r.t.)	>99	**15**	**16**	<1	96
2	**5**	$TiCl_4$	CH_2Cl_2	40 min (-78°C)	>99			<1	91
3	**5**	$MeOH/H_2SO_4$	MeOH	30 min (r.t.)	>99	**17**	**18**	<1	97
4	**5**	$MeOH/LiClO_4$	MeOH	18 h (80°C)	>99			<1	91
5	**5**	$MeOH/LiClO_4$	MeCN	18 h (80°C)	>99			<1	90
6	**5**	NaN_3/NH_4Cl	$MeOH:H_2O$ 8:1	18 h (80°C)	>99	**19**	**20**	<1	97
7	**5**	$NaN_3/LiClO_4$	MeCN	18 h (80°C)	91			9	94
8	**5**	$NaN_3/Mg(ClO_4)_2$	MeCN	18 h (80°C)	98			2	85
9	**5**	$NaN_3/Zn(OTf)_2$	MeCN	18 h (80°C)	97			3	80
10	**5**	LiN_3	MeCN	18 h (80°C)	83			17	93
11	**5**	$NHEt_2$	EtOH	3 days (80°C)	>99	**21**	**22**	<1	48
12	**5**	$NHEt_2/LiClO_4$	MeCN	18 h (80°C)	60			40	92
13	**5**	$PhSH/NEt_3$	MeOH	18 h (r.t.)	>99	**23**	**24**	<1	95
14	**5**	$PhSH/LiClO_4$	MeCN	18 h (80°C)	48			52	97
15	**5**	Me_2CuLi	Et_2O	5 h (-15 - 0°C)	70	**25**	**26**	30	99
16	**5**	$Al(Me)_3$	pentane	18 h (r.t.)	99			1	92
17	**5**	$Al(Me)_3$/crown	pentane	18 h (r.t.)	99			1	83
18	**5**	$LiAlH_4$	pentane	1 h (r.t.)	68	**27**	**28**	32	97
19	**5**	$LiAlH_4$/crown	pentane	5 h (r.t.)	87			13	81
20	**7**	NaN_3/NH_4Cl	$MeOH:H_2O$ 8:1	18 h (80°C)	>99	**29**	**30**	<1	96
21	**7**	$NaN_3/LiClO_4$	MeCN	18 h (80°C)	>99			<1	93
22	**7**	LiN_3	MeCN	18 h (80°C)	75			25	96
23	**7**	$NHEt_2$	EtOH	3 days (80°C)	>99	**31**	**32**	<1	87
24	**7**	$NHEt_2/LiClO_4$	MeCN	18 h (80°C)	77			23	93
25	**7**	$PhSH/NEt_3$	MeOH	18 h (r.t)	>99	**33**	**34**	<1	90
26	**7**	$PhSH/LiClO_4$	MeCN	18 h (80°C)	75			25	95
27	**7**	$Al(Me)_3$	pentane	18 h (r.t.)	>99	**35**	**36**	<1	95
28	**7**	$Al(Me)_3$/crown	pentane	18 h (r.t.)	>99			<1	80
29	**7**	$LiAlH_4$	pentane	1 h (r.t.)	83	**37**	**38**	17	97
30	**7**	$LiAlH_4$/crown	pentane	18 h (r.t.)	90			10	79

The complete C-1 regioselectivity observed in the reactions of the cis epoxide **5** under standard non-chelating conditions may be rationalized on the basis of conformational considerations and of the inductive effect of the substituent (OBn group). The cis epoxide **5**, reacting in its more stable conformation **5a** (vide infra), will be attacked by the nucleophile at the C-(1) oxirane carbon, in accordance with the diaxial opening rule (the Fürst-Plattner rule). Moreover, this position also appears to be less disfavored by the electron-withdrawing inductive effect of the heterofunctionality. Under these conditions, there was no apparent reason for epoxide **5** to react in its less stable conformation **5b**: the subsequent attack on the oxirane C-(2) carbon does not appear to be justified and *C-2 products* should not be correspondingly obtained, as experimentally observed (Scheme 3, and Table 1). When a metal ion is present in the opening reaction mixture (chelating conditions), the presence of *C-2 products*, in substantially quantities in some cases, may be attributed to the incursion of bidentate chelate structures of type **68** ($X=CH_2$). In these conditions, the initial complexation of the metal ion with the OBn functionality of **5**, in both conformation **a** and **b** to give **66** ($X=CH_2$) and **67** ($X=CH_2$), respectively, is presumably followed by an entropically favored further coordination of the metal with the oxirane oxygen to give, to a certain extent, the chelate structure **68** ($X=CH_2$) in which epoxide **5** is forced necessarily to adopt the less stable conformation **5b**. In accordance with the Fürst-Plattner rule, the attack of the nucleophile on the chelate structure **68** ($X=CH_2$) can only occur at the C-(2) carbon to yield different amounts of *C-2 products*, as experimentally found. Actually the increase in C-2 selectivity so far observed, is not so large as expected on the basis of the results obtained with the structurally related cis epoxide **1**, and of the analogies between the two chelate structures **69** and **68** from epoxides **1** and **5**, respectively. However, in the case of **68** ($X=CH_2$), the contemporary incursion of the following two factors, reasonably diminishes the reactivity of the C-(2) position of the chelate structure **68** towards the nucleophilic attack, while the same factors are not present to the same extent in the related chelate structure **69** from **1**: *i*) the closer vicinity in **68** than in **69** of the electron-withdrawing substituent (OBn) to the C-(2) oxirane carbon, and *ii*) all those stereoelectronic factors implied in the chelation-controlled ring opening of these systems.[11] As for factor *ii*, the attack of the nucleophile on C-(2) carbon of **68** ($X=CH_2$) necessarily makes the oxygen lone pair [ex-oxirane C(2)-O bond] unfavorably develop inside the six-membered ring C(1)-C(2)-C(3)-O-M^+-O to afford a situation of an unfavorable energy content. Actually, both factors *i* and *ii* have the effect of slowing down the reactivity of the chelate species **68** ($X=CH_2$) considerably, possibly making this species less effective than it could really be. The increase in C-2 selectivity obtained with the cis epoxide **5**, under chelate opening conditions is not general, but it appears to largely depend on the type of the attacking nucleophile: while nucleophiles such as N_3^-, $NHEt_2$ and PhSH give an interesting (N_3^-) and in some cases a remarkable ($NHEt_2$, and PhSH) increase in C-2 selectivity, nucleophiles such as MeOH and Cl^- give complete C-1 selectivity under any reaction conditions used (entries 2,4,7,10,12 and 14, Table 1). Evidently, the reactivity of the chelate species **68** ($X=CH_2$) is strongly influenced by the strength of the attacking nucleophile: only strong nucleophiles (N_3^-, NHR_2 and PhSH) are able, even if to a different extent, to attack it at the unfavorable C-(2) oxirane carbon (see above) to give significant amounts of C-2 selectivity, which almost parallel the relative nucleophilic strength (Scheme 3 and Table 1). Due to the presence in the reaction medium of a metal species (lithium or aluminum), the opening reactions of **5** with Me_2CuLi, $AlMe_3$ and

SCHEME 3

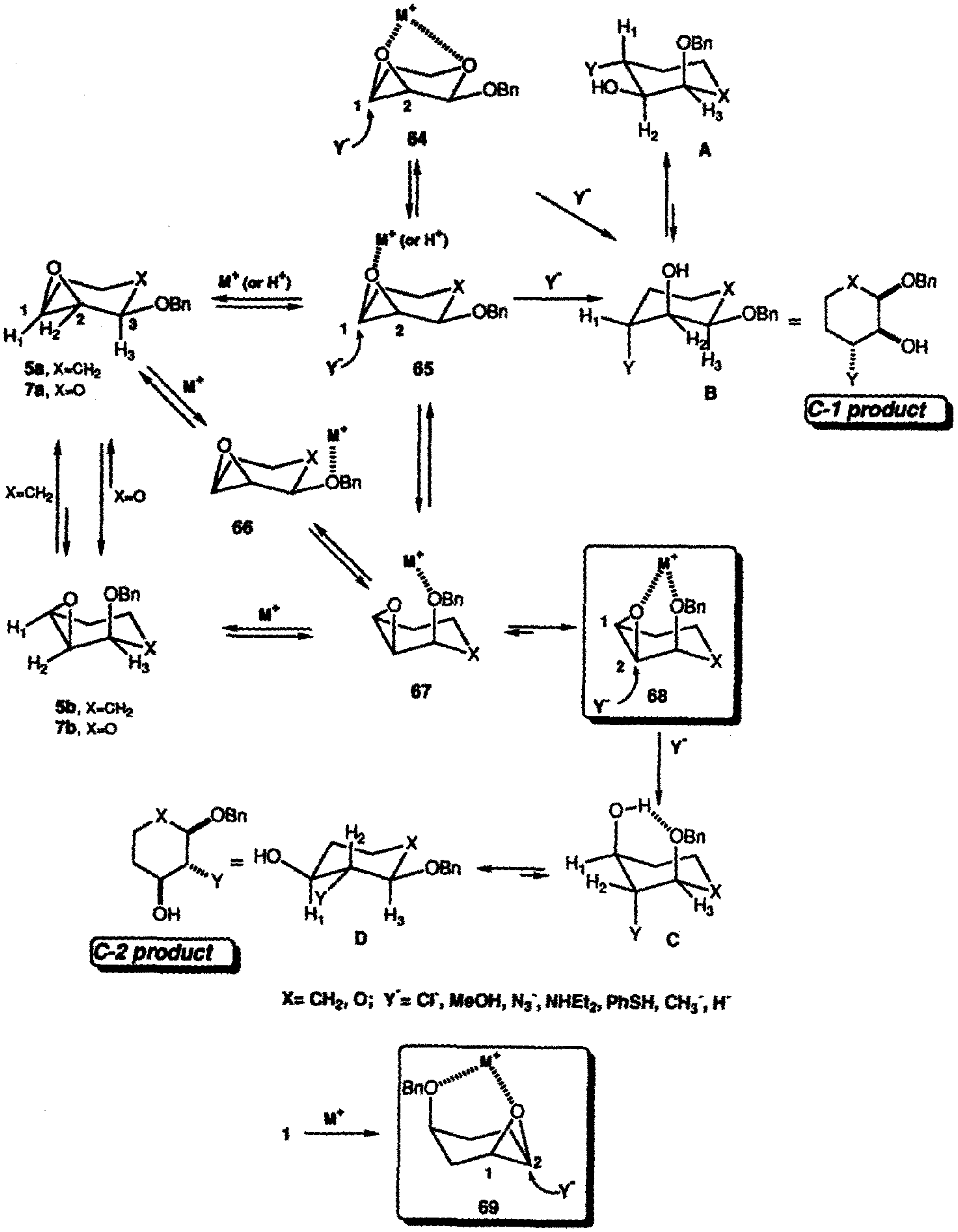

64
A
5a, X=CH2
7a, X=O
65
B
C-1 product
66
M+ (or H+)
Y-
M+
X=CH2
X=O
5b, X=CH2
7b, X=O
67
68
C
D
C-2 product
X= CH2, O; Y- = Cl-, MeOH, N3-, NHEt2, PhSH, CH3-, H-
1
69

Table 2. Regioselectivity of the Ring Opening Reactions of the trans Epoxides 6 and 8 Under Non-Chelating and Chelating Conditions.

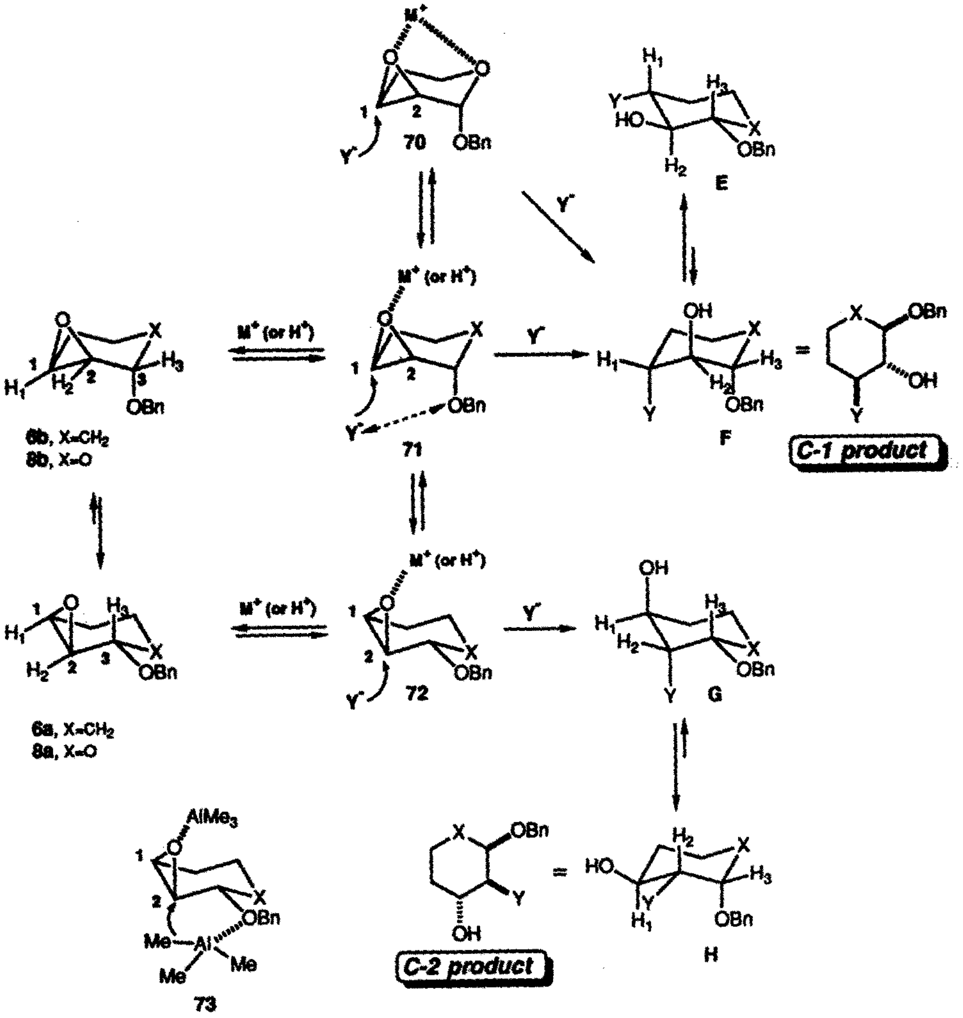
entry	epoxide	reagents	solvent	reaction time and temperature	*C-1 product*			*C-2 product*	yield %
1	**6**	HCl	$CHCl_3$	10 min (r.t.)	89	**39**	**40**	11	92
2	**6**	$TiCl_4$	CH_2Cl_2	40 min (-78°C)	52			48	93
3	**6**	$MeOH/H_2SO_4$	MeOH	30 min (r.t.)	>99	**41**	**42**	<1	91
4	**6**	$MeOH/LiClO_4$	MeOH	18 h (80°C)	>99			<1	89
5	**6**	NaN_3/NH_4Cl	$MeOH:H_2O$ 8:1	18 h (80°C)	83	**43**	**44**	17	95
6	**6**	$NaN_3/LiClO_4$	MeCN	18 h (80°C)	84			16	92
7	**6**	$NHEt_2$	EtOH	3 days (80°C)	>99	**45**	**46**	<1	90
8	**6**	$NHEt_2/LiClO_4$	MeCN	18 h (80°C)	>99			<1	91
9	**6**	$PhSH/NEt_3$	MeOH	18 h (r.t.)	86	**47**	**48**	14	92
10	**6**	$PhSH/LiClO_4$	MeCN	18 h (80°C)	85			15	90
11	**6**	Me_2CuLi	Et_2O	24 h (r.t.)	63	**49**	**50**	37	95
12	**6**	$Al(Me)_3$	pentane	18 h (r.t.)	<1			>99	90
13	**6**	$Al(Me)_3$/crown	pentane	18 h (r.t.)	76			24	85
14	**6**	$LiAlH_4$	pentane	1 h (r.t.)	70	**51**	**52**	30	98
15	**6**	$LiAlH_4$/crown	pentane	5 h (r.t.)	77			23	82
16	**8**	NaN_3/NH_4Cl	$MeOH:H_2O$ 8:1	18 h (80°C)	>99	**53**	**54**	<1	94
17	**8**	$NaN_3/LiClO_4$	MeCN	18 h (80°C)	>99			<1	91
18	**8**	$NHEt_2$	EtOH	3 days (80°C)	>99	**55**	**56**	<1	91
19	**8**	$NHEt_2/LiClO_4$	MeCN	18 h (80°C)	>99			<1	89
20	**8**	$PhSH/NEt_3$	MeOH	18 h (r.t.)	>99	**57**	**58**	<1	89
21	**8**	$PhSH/LiClO_4$	MeCN	18 h (80°C)	>99			<1	94
22	**8**	$Al(Me)_3$	pentane	18 h (r.t.)	>99	**59**	**60**	<1	92
23	**8**	$Al(Me)_3$/crown	pentane	18 h (r.t.)	>99			<1	81
24	**8**	$LiAlH_4$	pentane	1 h (r.t.)	>99	**61**	**62**	<1	98
25	**8**	$LiAlH_4$/crown	pentane	18 h (r.t.)	>99			<1	80

$LiAlH_4$ must be considered, for our purposes, as carried out under chelating conditions.[12] Accordingly, the use in the $LiAlH_4$ reduction of a metal-sequestering agent such as 12-crown-4 ether leads to an enhancement in the C-1 selectivity, in accordance with the proposed rationalization (Scheme 3 and Table 1).

Under standard conditions, the behavior of the cis epoxide **7** is substantially analogous to that observed with epoxide **5**; also in this case, the complete C-1 selectivity observed can be rationalized on the basis of the strong electron-withdrawing inductive effect of the heterofunctionality (the acetalic group) which forces epoxide **7** to react through conformer **7a**, having the benzyloxy group equatorial, which is in the present case the less stable one (vide infra) (Scheme 3). In the reaction of the cis epoxide **7** under chelate conditions, two reasonable chelate species can be formed and be competitively present in the reaction medium: the chelate species **68** (X=O) (leading to *C-2 products*) of the same type as described above for the cis epoxide **5**, and the chelate species **64** (leading to *C-1 products*), in which the chelating metal is coordinated between the oxirane and the acetal oxygen of the tetrahydropyranyl ring.[5,13] However, due to the above-discussed electron-withdrawing properties of the substituent, which are particularly strong in the present case, the nucleophilic attack at the C-(1) carbon of **64** is more highly favored than the competing nucleophilic attack at the C-(2) carbon of **68** (X=O). As a consequence, also under chelating conditions a decided preference for *C-1 products* is to be expected, as experimentally found. In this situation, only strong nucleophiles such as PhSH and $NHEt_2$ are able to trap the less reactive chelate species of type **68** (X=O) efficiently, and a partial but significant C-2 selectivity (20-30%) can be consequently observed (Scheme 3 and Table 1).

The behavior of the trans epoxides **6** and **8** appears to be mostly driven by the electron-withdrawing inductive effect of the adjacent corresponding *O*-functionality. As a consequence, epoxides **6** and **8** are forced to react in their less stable conformation **6b** and **8b**, respectively, having the benzyloxy group axial, in order to allow diaxial opening of the oxirane ring at the less disfavored C-(1) oxirane carbon, giving a result of complete or almost complete C-1 selectivity both under standard and chelating reaction conditions (Scheme 4 and Table 2). However, in the reaction of epoxide **6** with negatively charged nucleophiles (Cl^-, N_3^-, PhS^-, Me^-, and H^-), the presence of an unfavorable interaction (as shown in structure **71**, Scheme 4) between the approaching nucleophile and the benzyloxy oxygen of **6**, reacting through conformation **6b**, can force epoxide **6** to react partially through its conformation **6a** (structure **72**, Scheme 4) to give some amounts of *C-2 products* as experimentally observed (Table 2). Interestingly, the methylation of **6** with $AlMe_3$ is even completely C-2 selective (entry 12, Table 2). Evidently, in this case, the incursion of an effective interaction between the alkylating reagent ($AlMe_3$) and the OBn functionality of the epoxide (as tentatively shown in structure **73**, Scheme 4) greatly favors nucleophilic attack on the close C-(2) oxirane carbon. However, the use in this reaction of the metal-complexing 12-crown-4 ether effectively prevents such an interaction and a more C-1 selective result is accordingly obtained in these conditions (entry 13, Table 2). In the case of the epoxide **8**, the much stronger electron-withdrawing effect of the two *O*-fuctionalities, dramatically favors the formation of *C-1 products*, to the point that they are the only reaction products. Unlike to epoxide **6** which cannot give, for structural reasons, any chelate species, the trans epoxide **8** can yield, under metal salt-promoted opening conditions, the chelate species of type **70**,[13] in which the endocyclic and the oxirane oxygens are involved in the chelation with the metal. However, in this case, the incursion of species of type **70**, which would favor the formation of *C-1 products*, has no appreciable effect on the regiochemical outcome

SCHEME 4



$X = CH_2, O$; $Y^- = Cl^-, MeOH, N_3^-, NHEt_2, PhSH, CH_3^-, H^-$

of the opening reaction of epoxide **8**, due to the complete C-1 selectivity already observed under standard conditions (Scheme 4 and Table 2).

Structures, Configurations, and Conformations

The structure and configuration of the known epoxides cis **5** and trans **6** had previously been firmly established.[6] The half-band width value ($W_{1/2}$=18.0 Hz in **5** and 16.1 Hz in **6**)[14] of the signal of the proton α to the OBn group in the ^{1}H NMR spectra of the two diastereoisomeric epoxides **5** and **6** indicates for both epoxides a conformational equilibrium in which the conformer **5a** and **6a**, respectively, with the substituent (OBn) in an equatorial position, prevails (Schemes 3 and 4). As for the diastereoisomeric pair of epoxides **7** and **8**, their structure and relative configuration was derived from the results of their LAH reduction (Tables 1 and 2). In fact, only epoxide **7** affords, even if in a small amount (17%), the alcohol **38**: the IR spectrum of a dilute CCl_4 solution of **38** exhibits a characteristic OH···O interaction (3548 cm^{-1}),[4b,c,15] which is possible only when a 1,3-cis relationship is present between the interacting groups, such as the hydroxyl and benzyloxy groups in **38**. Bearing in mind that the configuration of the alcohols obtained in the reduction of an epoxide must correspond to that of the starting compound, this result makes it possible to assign the cis and trans configuration unequivocally to diastereoisomeric epoxides **7** and **8**, respectively. Moreover, alcohol **38** is also obtained, together with alcohol **63** (Scheme 2),[1] in the LAH reduction of the regioisomeric cis epoxide **3**, whose structure and configuration had previously been established.[1] As for the conformational equilibrium in **7** and **8**, an examination of the ^{1}H NMR data, particularly of the multiplicity of the signal of the anomeric proton H_3 [a doublet in **7** ($J_{2,3}$=3.1 Hz), and a singlet in **8**], and of the molecular models, indicates for these epoxides a preference for conformers **7b** and **8a**, respectively. These results have been nicely confirmed by a conformational study carried out by means of PCMODEL program[16] which found for the minimum energy content conformation of epoxides **7** and **8** an H(2)-C(2)-C(3)-H(3) dihedral angle value of 25.4° and 100.8°, respectively, with corresponding $J_{2,3}$ values (4.6 Hz in **7** and 0.9 Hz in **8**) in agreement with the experimental results. Evidently, in these epoxides, the repulsive interaction between the endocyclic and the oxirane oxygen, present in conformers **7a** and **8b**, appears to be the dominating factor in determining the preferred conformation.[17]

The structures and configurations of the opening products obtained as regioisomeric pairs (*C-1* and *C-2 products*) in the above-mentioned opening reactions of both the cis **5** and **7** and the trans epoxides **6** and **8** were unequivocally determined by simple considerations based on the configuration of the starting epoxide, the anti stereoselectivity commonly observed in the opening reactions of typically aliphatic and cycloaliphatic epoxides under the conditions used,[1,4,5,18] an examination of their ^{1}H NMR spectra [coupling constants and/or half-bandwidth ($W_{1/2}$)[14] of the signal of the protons α to OH, Y and OBn groups (protons H_1, H_2, and H_3, Schemes 3 and 4 and Table 3)], and, finally, by the use of appropriate double resonance experiments carried out on their monoacetyl derivatives. In the case of *C-2 products* from the cis epoxides **5** and **7** [azido

Table 3. Spectroscopic Data for Compounds 15-61.[a]

	^{1}H NMR δ			IR (CCl_4) (OH stretching), cm^{-1}		
compd	H_1 ($W_{1/2}$,Hz)^{b,c}	H_2 ($W_{1/2}$,Hz)^{b,c}	H_3 ($W_{1/2}$, or J, Hz)^{d}	1,2 OH···Y	1,3 OH···O	free OH
15	4.13 (18.0)^{b,e}	3.64 (14.0)^{c,f}	3.91 (10.0)^{g}	3585^{k,o}		
17	3.61 (14.5)^{b,e}	3.42 (18.0)^{c,e}	3.82 (11.0)^{g}	3589^{l,o}		
19	3.50 (24.0)^{b,g}	3.36 (15.0)^{c,f}	3.72 (10.0)^{e}	3570^{m,o}		
20	*h*	*h*	*h*	3593^{m}	3540^{q}	
21	3.03 (26.0)^{b,g}	3.39 (15.2)^{c,f}	4.00 (9.5)^{e}	3423^{m}		
22	3.18 (22.0)^{c,e}	2.45 (19.0)^{b,i}	3.47 (22.0)^{e}	3425^{m}		
23	3.35 (17.2)^{b,e}	3.52 (15.0)^{c,f}	3.81 (11.0)^{g}	3576^{n,o}		
24	3.53 (13.0)^{c,e}	3.07 (17.4)^{b,i}	3.39 (19.5)^{g}		3531^{r}	
25		3.04 (22.0)^{c,e}	3.67 (7.5)^{e}	3582^{p}		
26	3.03 (20.7)^{c,g}		3.23 (20.7)^{g}		3532^{s}	3633^{s}
27		3.44 (16.3)^{c,e}	3.78 (14.5)^{e}	3584^{p}		
28	3.46 (18.5)^{c,e}		3.65 (18.5)^{e}		3538^{s}	3618^{s}
29	*h*	*h*	4.88 (J=3.6)^{j}	3574^{m,o}		
30	*h*	3.20 (17.3)^{b,f}	4.28 (J=7.1)^{j}	3597^{m,s}	3539^{q}	
31	3.16 (23.0)^{b,e}	3.53 (15.2)^{c,f}	5.09 (J=3.5)^{j}	3468^{m} 3582^{p,q}		
32	3.50 (18.8)^{c,g}	2.44 (18.8)^{b,f}	4.41 (J=8.5)^{j}	3462^{m}		
33	*h*	*h*	4.88 (J=3.3)^{j}	3576^{n,o}		
34	3.74 (15.6)^{c,e}	3.09 (15.6)^{b,i}	4.60 (J=4.9)^{j}		3539^{r}	
35		3.07 (18.8)^{c,e}	4.78 (J=3.5)^{j}	3583^{p}		
37	*h*	*h*	4.82 (J=3.2)^{j}	3588^{p}		
39	3.65 (25.0)^{b,e}	3.43 (19.4)^{c,i}	3.16 (25.0)^{e}	3593^{k,o}		
40	*h*	*h*	*h*	3597^{k}		
41	*h*	*h*	*h*	3591^{l,o}		
43	*h*	3.40 (19.0)^{b,h}	*h*	3599^{m,o}		
44	*h*	3.17 (13.7)^{a,e}	*h*	3601^{m}		
45	3.18 (14.0)^{b,e}	*h*	*h*	3427^{m}		
47	2.81 (21.7)^{b,e}	*h*	*h*	3589^{n,o}		
48	3.85 (24.4)^{c,f}	2.97 (16.0)^{b,f}	3.95 (8.2)^{e}	3582^{n}		
49		3.00 (18.7)^{c,i}	3.14 (24.8)^{e}	3593^{p}		
50	3.69 (23)^{c,g}		3.64 (9.3)^{e}			3622
51		3.14 (21.0)^{c,e}	3.43 (21.0)^{e}	3593^{p}		
52	3.74 (14.0)^{b,e}		4.00 (17.5)^{e}			3620
53	*h*	*h*	4.17 (J=7.2)^{j}	3609^{m,o}		

55	*h*	3.98 (19.6)[c,e]	4.25 (*J*=7.3)[j]	3472[m] 3599[p]
57	3.34 (21.0)[b,e]	2.96 (28.0)[c,e]	4.32 (*J*=7.1)[j]	3603[n,o]
59		3.04 (19.1)[b,f]	4.21 (*J*=7.4)[j]	3605[p]
61		*h*	4.30 (*J*=5.5)[j]	3602[p]

Compounds **16, 18, 36, 38, 42, 46, 54, 56, 58, 60, 62** (Scheme 2) were not isolated because not present in the ring-opening reactions of epoxides **5-8**. [b] CHY, [c] C*H*OH, [d] C*H*OBn (see Schemes 1, 3, and 4). [e] Multiplet. [f] Doublet of doublets. [g] Doublet of doublets of doublets. [h] The signal overlaps with other signals. [i] Triplet. [j] Doublet. [k] Y=Cl. [l] Y=O [m] Y=N. [n] Y=S. [o] The band could be also attributed to an 1,2 OH···OBn interaction. [p] 1,2 OH···OBn. [q] Weak band. [r] Broad band. [s] Strong band.

alcohol **20**, thioalcohols **24** and **34**, and alcohols **28** and **38**,[1] with the only exception of the amino alcohols **22** and **32**] the structure assigned was unequivocally confirmed by the presence of a 1,3 OH···O interaction in the IR spectra of these compounds in dilute CCl_4 solution (Table 3 and Scheme 3).[4b,c,15] In these compounds, with the only exception of thioalcohols **24** and **34** which exist predominantly in a conformation like **C** (Scheme 3), the contemporary presence in the IR spectra of a free OH or a 1,2 OH···Y indicates the existence of a conformational equilibrium in which both conformer **C** and **D** are present (Table 3 and Scheme 3).[19] In the case of *C-1 products*, both from cis **5** and **7** and trans epoxides **6** and **8**, the presence of a 1,2 OH···Y hydrogen bond, and the mostly equatorial (*C-1 products* from cis epoxides **5** and **7**) or axial (*C-1 products* from trans epoxides **6** and **8**) nature[14] of proton H_3 indicate for these compounds a conformational equilibrium in which conformers **A** (*C-1 products* from **5** and **7**) and **E** (*C-1 products* from **6** and **8**) appear to be the most commonly present (Table 3 and Schemes 3 and 4).

Experimental

For general experimental procedure see ref. 4c and 5.

cis-2,3-Epoxy-1-benzyloxycyclohexane (5). Following a previously described procedure,[6] treatment at 0°C of 2-cyclohexen-1-ol (2.25 g, 23.0 mmol) in CH_2Cl_2 (140 ml) with 55% *m*-CPBA (7.90 g, 25.2 mmol) afforded a crude reaction product (2.14 g) consisting of a 96:4 mixture of epoxy alcohols cis **9** and trans **10** (GC, and ^1H NMR) which was directly used in the next step.

A solution of the above crude reaction product (2.14 g, 18.7 mmol) in anhydrous THF (22 ml) was added to a stirred suspension containing NaH (1.12 g of a 80% dispersion in mineral oil, 37.4 mmol) and benzyl bromide (3.08 g, 18.0 mmol) in anhydrous THF (50 ml) maintained at 50°C. The resulting reaction mixture was stirred for 18 h at 55-60°C. After cooling, water was added in order to destroy the excess of hydride. Dilution with ether (150 ml) and evaporation of the washed (water) organic solution afforded a crude reaction product (3.70 g) consisting of a 96:4 mixture of epoxides cis **5** and trans **6** (GC and ^1H NMR), which was filtered on a short silica gel column. Elution with petroleum ether afforded a crude liquid consisting of cis epoxide **5** (3.2 g) (GC) which was distilled to give pure **5**, as a liquid: b.p. 98-100°C (0.3 mmHg): ^1H NMR ($CDCl_3$) δ 7.14-7.36 (m, 5H), 4.61 (s, 2H), 3.68-3.76 (m, 1H, $W_{1/2}$=18.0 Hz, H_3), 3.17-3.35 (m, 2H), 1.68-1.85 (m, 2H), 1.42-1.65 (m, 2H), 1.05-1.30 (m, 2H). Anal.Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.59; H, 7.63.

trans-2,3-Epoxy-1-benzyloxycyclohexane (6). Proceeding as above described for the preparation of **5**, alkylation of 2-cyclohexen-1-ol (2.0 g, 20.4 mmol) with benzylbromide (3.42 g, 20.0 mmol) in the presence of NaH (1.20 g of a 80% dispersion in mineral oil, 40.0 mmol) afforded crude ether **11** (4.0 g) which was purified by filtration through a short silica gel column. Elution with petroleum ether afforded pure **3-benzyloxycyclohexene (11)** (3.30 g), as a liquid: ^{1}H NMR ($CDCl_3$) δ 7.10-7.48 (m, 5H), 5.76-5.91 (m, 2H), 4.59 and 4.56 (ABdd, 2H, *J*=12.0 Hz), 3.92-3.97 (m, 1H), 1.49-2.15 (m, 6H). Anal. Calcd for $C_{13}H_{16}O$; C, 82.93; H, 8.56. Found: C, 82.74; H, 8.41.

A solution of **11** (3.30 g, 17.5 mmol) in CH_2Cl_2 (100 ml) was treated at 0°C under stirring with 55% *m*-CPBA (5.53 g, 17.7 mmol). When all the olefin was reacted (TLC), the reaction mixture was washed (10% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, 5% aqueous NaOH, and water) and the solvent evaporated to give an oily residue (3.50 g) consisting of a 73:27 mixture of epoxides trans **6** and cis **5** (GC and ^{1}H NMR). This crude product was subjected to flash chromatography using a 9:1 mixture of hexane and AcOEt as the eluant to yield pure cis epoxide **5** (0.75 g) and trans epoxide **6** (2.15 g), as a liquid: ^{1}H NMR ($CDCl_3$) δ 7.18-7.30 (m, 5H), 4.57 (s, 2H), 3.61-3.80 (m, 1H, $W_{1/2}$= 16.1 Hz, H_3), 3.08-3.30 (m, 2H), 1.10-2.05 (m, 6H). Anal.Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.41; H, 7.94.

2-Benzyloxy-5,6-dihydro-2*H*-pyran (14). Following a previously described procedure,[7] treatment of a solution of phenylselenyl chloride (5.25 g, 27.5 mmol) with 3,4-dihydro-2*H*-pyran (**12**) (2.10 g, 25.0 mmol) and a solution of benzyl alcohol (4.54 g, 42.5 mmol) and triethylamine (3.78 g, 37.5 mmol) afforded a crude reaction mixture (8.5 g) which was filtered through a short silica gel column. Elution with a 95:5 mixture of petroleum ether and ether afforded a yellow liquid product (6.44 g) consisting of **trans-2-benzyloxy-3-(phenylseleno)tetrahydropyran (13)**[7] which was not furtherly purified: ^{1}H NMR ($CDCl_3$) δ 7.53-7.46 (m, 2H), 7.16-7.36 (m, 8H), 4.80 and 4.53 (ABdd, 2H, *J*=11.8 Hz), 4.72 (d, 1H, *J*=4.7 Hz, C*H*OBn), 3.90-4.00 (m, 1H), 3.50-3.61 (m, 1H), 3.32-3.39 (m, 1H), 2.18-2.30 (m, 1H), 1.48-1.91 (m, 3H). Anal.Calcd for $C_{18}H_{20}O_2Se$: C, 62.24; H, 5.80. Found: C, 62.36; H, 6.01.

The above crude product (6.44 g, 18.5 mmol) in CH_2Cl_2 (50 ml) in the presence of pyridine (2.43 ml, 30.3 mmol) was dropwise treated at 0°C with 35% aqueous H_2O_2 (3.88 ml, 40.0 mmol) and the resulting reaction mixture was stirred at r.t. for 6 days.[8] Evaporation of the washed (saturated aqueous $NaHCO_3$ and water) organic solution afforded a crude reaction product which was chromatographed through a silica gel column. Elution with a 95:5 mixture of petroleum ether and AcOEt afforded pure olefin **14** (2.70 g), as a liquid: ^{1}H NMR ($CDCl_3$) δ 7.24-7.40 (m, 5H), 6.01-6.10 (m, 1H), 5.71-5.80 (m, 1H), 5.01 (s, 1H, C*H*OBn), 4.80 and 4.58 (ABdd, 2H, *J*=11.9 Hz), 4.00 (ddd, 1H, *J*=11.3 and 3.7 Hz), 3.76 (dd, 1H, *J*=11.4 and 6.1 Hz), 2.23-2.42 (m, 1H), 1.91 (dt, 1H, *J*=17.7, and 5.4 Hz). Anal.Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.41. Found: C, 75.79; H, 7.26.

Synthesis of Epoxides cis 7 and trans 8. a) Following a previously described procedure,[9] a stirred suspension of olefin **14** (1.52 g, 8.0 mmol), benzonitrile (1.24 ml, 12.0 mmol) and K_2CO_3 (0.20 g) in MeOH (4.0 ml) was dropwise treated at r.t. with 35% aqueous H_2O_2 (0.97 ml, 10.0 mmol) to yield a crude liquid product (1.20 g) consisting of a 43:57 mixture of epoxides cis **7** and trans **8** (GC) which was subjected to flash chromatography with a 95:5 mixture of hexane and AcOEt as the eluant, to give pure epoxides **7** (0.46 g) and **8** (0.61 g).

cis 2-Benzyloxy-3,4-epoxytetrahydropyran (7), a liquid: ^{1}H NMR ($CDCl_3$) δ 7.19-7.34 (m, 5H), 4.93 (d, 1H, *J*=3.1 Hz, H_3) 4.75 and 4.55 (ABdd, 2H, *J*=12.3 Hz), 3.73-3.86 (m, 1H), 3.28-3.42 (m, 2H), 3.19 (unresolved triplet, 1H, *J*=3.5 Hz), 1.87-1.93 (m, 2H). Anal.Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.75; H, 6.71.

trans 2-Benzyloxy-3,4-epoxytetrahydropyran (8), a solid, mp 38-39°C: ^{1}H NMR ($CDCl_3$) δ 7.26-7.39 (m, 5H), 5.03 (s, 1H, H_3), 4.80 and 4.57 (ABdd, 2H, *J*=11.6 Hz), 3.64-3.89 (m, 2H), 3.32-3.48 (m, 2H), 2.02-2.20 (m, 1H), 1.72-1.94 (m, 1H). Anal.Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.64; H, 6.59.

a) A solution of olefin **14** (0.57 g, 3.0 mmol) in CH_2Cl_2 (30 ml) was treated at 0°C with 55% *m*-CPBA (1.11 g, 3.3 mmol). After 24 h, usual workup afforded a crude reaction product (0.56 g) consisting of a 25:75 mixture of diastereoisomeric epoxides cis **7** and trans **8** (GC) which was subjected to preparative TLC (a 85:15 mixture of petroleum ether and AcOEt was used as the eluant). Extraction with cold $CHCl_3$ of the two most intense bands afforded pure epoxides cis **7** (0.080 g) and trans **8** (0.25 g).

c) A solution of olefin **14** (0.095 g, 0.50 mmol) in a 3:1 THF/H_2O mixture (6.0 ml) was treated at r.t. with N-bromosuccinimide (NBS) (0.107 g, 0.60 mmol) and the reaction mixture was left for 18 h at the same temperature. Dilution with water, extraction with ether and evaporation of the washed (water) ether extracts afforded a crude reaction product (0.13 g) [IR (neat) 3421 cm^{-1} (OH)] which was dissolved in anhydrous benzene (10 ml) and treated with *t*-BuOK (0.056 g, 0.50 mmol x 2). After 1 h stirring at r.t., evaporation of the filtered organic solution afforded a crude liquid reaction product consisting of a 37:63 mixture of epoxides cis **7** and trans **8** (GC).

Reaction of Epoxides 5 and 6 with HCl in $CHCl_3$. The following procedure is typical. A solution of the cis epoxide **5** (0.102 g, 0.50 mmol) in $CHCl_3$ (20 ml) was treated at r.t. with 36% aqueous HCl (5.0 ml) and the reaction mixture was stirred for 15 min at the same temperature. Evaporation of the washed (saturated aqueous $NaHCO_3$ and water) organic solution afforded a crude reaction product (0.115 g) consisting of practically pure chlorohydrin **15** which was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-2-benzyloxy-*t*-6-chloro-*r*-1-cyclohexanol (15)** (0.085 g), as a liquid: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.25-7.45 (m, 5H), 4.62 and 4.51 (ABdd, 2H, *J*=11.7 Hz), 4.13 (sextet, 1H, *J*=4.2 Hz, H_1), 3.91 (ddd, 1H, *J*=5.7 and 2.9 Hz, H_3), 3.64 (dd, 1H, *J*=8.3 and 3.1 Hz, H_2), 2.07-2.25 (m, 1H), 1.86-2.07 (m, 1H), 1.40-1.79 (m, 4H). Anal.Calcd for $C_{13}H_{17}ClO_2$: C, 64.86; H, 7.11. Found: C, 64.75; H, 7.34. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.18-7.27 (m, 5H), 4.88 (dd, 1H, *J*=9.0 and 2.8 Hz, $W_{1/2}$=15.0 Hz, C*H*OAc), 4.51 and 4.43 (ABdd, 2H, *J*=12.0 Hz), 4.28 (sextet, 1H, *J*=4.4 Hz, $W_{1/2}$=19.0 Hz, CHCl), 3.85 (ddd, 1H, *J*=5.7 and 2.7 Hz, $W_{1/2}$=9.4 Hz, C*H*OBn), 2.03 (s, 3H), 2.05-2.20 (m, 1H), 1.78-1.93 (m, 1H), 1.39-1.72 (m, 4H). Anal.Calcd for $C_{15}H_{19}ClO_3$: C, 63.71; H, 6.77. Found: C, 63.89; H, 6.51.

The crude reaction product (0.114 g) from the trans epoxide **6** was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-benzyloxy-*t*-6-chloro-*r*-1-cyclohexanol (39)** (0.071 g), as a solid, mp 35-36°C; IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.17-7.28 (m, 5H), 4.61 and 4.53 (ABdd, 2H, *J*=11.8 Hz), 3.57-3.70 (m, 1H, H_1), 3.43 (unresolved triplet, 1H, *J*=9.7 Hz, H_2), 3.10-3.22 (m, 1H, H_3), 1.98-2.13 (m, 2H), 1.48-1.73 (m, 2H), 1.09-1.34 (m, 2H). Anal.Calcd for $C_{13}H_{17}ClO_2$: C, 64.86; H, 7.11. Found: C, 64.66; H, 6.95. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.24-7.35 (m, 5H), 5.03 (unresolved triplet, 1H, *J*=9.6 Hz, $W_{1/2}$=21.7 Hz, C*H*OAc), 4.61 and 4.49 (ABdd, 2H, *J*=12.1 Hz), 3.71 (m, 1H, $W_{1/2}$= 24.0 Hz, CHCl), 3.30 (m, 1H, $W_{1/2}$=24.0 Hz, C*H*OBn), 1.98-2.25 (m, 1H), 2.08 (s, 3H), 1.15-1.86 (m, 4H). Anal.Calcd for $C_{15}H_{19}ClO_3$: C, 63.71; H, 6.77. Found: C, 63.94; H, 6.71.

Reaction of Epoxides 5 and 6 with $TiCl_4$. General procedure. A solution of the epoxide (0.102 g, 0.5 mmol) in anhydrous CH_2Cl_2 (10 ml) was treated at -78°C with 1M $TiCl_4$ in CH_2Cl_2 (0.55 ml). The reaction mixture was stirred at the same temperature for 30 min, then slowly warmed to 0°C. Evaporation of the washed (saturated aqueous $NaHCO_3$) organic solution afforded a crude reaction product which was analyzed by GC and ^1H NMR (Tables 1 and 2).

The crude reaction product (0.110 g) from the cis epoxide **5** was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure chlorohydrin **15** (GC and ^1H NMR).

The crude reaction mixture (0.112 g) from the trans epoxide **6** was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands afforded pure chlorohydrin **39** (0.045 g) and ***t*-3-benzyloxy-*t*-2-chloro-*r*-1-cyclohexanol (40)** (0.040 g), as a liquid: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.17-7.34 (m, 5H), 4.54 and 4.53 (ABdd, 2H, *J*=11.0 Hz), 3.75-3.99 (m, 3H), 1.85-2.10 (m, 2H), 1.10-1.72 (m, 2H). Anal.Calcd for $C_{13}H_{17}ClO_2$: C, 64.86; H, 7.11. Found: C, 64.77; H, 7.26. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.24-7.39 (m, 5H), 5.17 (ddd, 1H, *J*=9.6 and 4.4 Hz, $W_{1/2}$=17.8 Hz, C*H*OAc), 4.60 and 4.61 (ABdd, 2H, *J*=11.9 Hz), 4.07 (dd, 1H, *J*=7.7 and 3.0 Hz, $W_{1/2}$=13.5 Hz, CHCl), 3.85 (ddd, 1H, *J*=6.8 and 2.7 Hz, $W_{1/2}$=11.0 Hz, C*H*OBn), 2.04 (s, 3H), 1.21-2.16 (m, 6H). Anal.Calcd for $C_{15}H_{19}ClO_3$: C, 63.71; H, 6.77. Found: C, 63.54; H, 6.51.

H^+-Catalyzed Methanolysis of Epoxides 5 and 6. General procedure. A solution of the epoxide (0.102 g, 0.50 mmol) in 0.2 N H_2SO_4 in anhydrous MeOH (10 ml) was stirred at r.t for 30 min. Dilution with water, extraction with ether and evaporation of the washed (saturated aqueous $NaHCO_3$, and water) ether extracts afforded a crude liquid product which was analyzed by GC and ^1H NMR (Tables 1 and 2).

The crude product (0.115 g) from the cis epoxide **5** was purified by semipreparative TLC (a 7: 3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-2-benzyloxy-*t*-6-methoxy-*r*-1-cyclohexanol (17)** (0.078 g), as a liquid: IR, see Table 3; ^1H NMR

(CDCl$_3$) δ 7.26-7.37 (m, 5H), 4.62 and 4.54 (ABdd, 2H, J=11.7 Hz), 3.82 (ddd, 1H, J=8.6 and 3.0 Hz, H$_3$), 3.57-3.68 (m, 1H, H$_1$), 3.40 (s, 3H), 3.34-3.50 (m, 1H, H$_2$), 1.80-2.08 (m, 2H), 1.18-1.65 (m, 4H). Anal.Calcd for $C_{14}H_{20}O_3$: C, 71.15; H, 8.53. Found: C, 71.37; H, 8.65. **Acetate**, a liquid: ^{1}H NMR (CDCl$_3$) δ 7.13-7.26 (m, 5H), 4.93 (dd, 1H, J=7.4 and 2.9 Hz, $W_{1/2}$=11.3 Hz, C*H*OAc), 4.46 (s, 2H), 3.67-3.76 (m, 1H, $W_{1/2}$=11.3 Hz, C*H*OBn), 3.49 (ddd, 1H, J=7.5 and 4.2 Hz, $W_{1/2}$= 15.0 Hz, C*H*OMe), 3.27 (s, 3H), 2.01 (s, 3H), 1.66-1.88 (m, 2H), 1.28-1.60 (m, 4H). Anal.Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.96. Found: C, 69.26; H, 8.11.

The crude reaction product (0.108 g) from the trans epoxide **6** was purified by semipreparative TLC (a 7: 3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-benzyloxy-*t*-6-methoxy-*r*-1-cyclohexanol (41)** (0.090 g), as a liquid: IR, see Table 3; ^{1}H NMR (CDCl$_3$) δ 7.19-7.50 (m, 5H), 4.63 and 4.53 (ABdd, 2H, J=11.7 Hz), 3.36 (s, 3H), 3.12-3.45 (m, 2H), 2.89-3.04 (m, 1H), 1.05-2.12 (m, 6H). Anal.Calcd for $C_{14}H_{20}O_3$: C, 71.15; H, 8.53. Found: C, 71.39; H, 8.27. **Acetate**, a liquid: ^{1}H NMR (CDCl$_3$) δ 7.27-7.33 (m, 5H), 4.85 (unresolved triplet, 1H, J=9.4 Hz, $W_{1/2}$=20.7 Hz, C*H*OAc), 4.63 and 4.49 (ABdd, 2H, J=11.7 Hz), 3.34 (s, 3H), 3.18-3.44 (m, 1H, $W_{1/2}$=21.0 Hz, CHO), 2.95-3.13 (m, 1H, $W_{1/2}$=25.0 Hz, CHO), 1.08-2.17 (m, 6H). Anal.Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.96. Found: C, 69.31; H, 7.85.

Methanolysis of Epoxides 5 and 6 in the Presence of LiClO$_4$. General procedure. The epoxide (0.102 g, 0.50 mmol) was added to a 17 M LiClO$_4$ solution in anhydrous MeOH and the reaction mixture was stirred at 80°C for 24 h. Dilution with ether and evaporation of the washed (water) ether solution afforded a crude reaction product which was analyzed by GC and ^{1}H NMR (Tables 1 and 2).

Azidolysis of Epoxides 5-8 with NaN$_3$-NH$_4$Cl. General procedure. A solution of the epoxide (0.50 mmol) in a 8:1 MeOH/H$_2$O mixture (3.0 ml) was treated with NaN$_3$ (0.162 g, 2.50 mmol) and NH$_4$Cl (0.058 g, 1.10 mmol) and the resulting reaction mixture was stirred at 80°C for 18 h. Dilution with ether and evaporation of the washed (water) organic solution afforded a crude reaction product which was analyzed by GC and ^{1}H NMR (Tables 1 and 2).

The crude reaction product (0.120 g) from the cis epoxide **5** was purified by semipreparative TLC (a 8: 2 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-azido-*c*-6-benzyloxy-*r*-1-cyclohexanol (19)** (0.085 g), as a liquid: IR, see Table 3; ^{1}H NMR (CDCl$_3$) δ 7.14-7.27 (m, 5H), 4.51 and 4.33 (ABdd, 2H, J=11.6 Hz), 3.68-3.77 (m, 1H, H$_3$), 3.50 (ddd, 1H, J=9.1 and 4.4 Hz, H$_1$), 3.35 (dd, 1H, J=8.9 and 3.1 Hz, H$_2$), 1.78-2.00 (m, 2H), 1.31-1.59 (m, 2H), 1.08-1.30 (m, 2H). Anal.Calcd for $C_{13}H_{17}N_3O_2$: C, 63.14; H, 6.92; N, 16.98. Found: C, 63.41; H, 6.95; N, 17.12. **Acetate**, a liquid: ^{1}H NMR (CDCl$_3$) δ 7.19-7.45 (m, 5H), 4.65 (dd, 1H, J=9.7 and 2.9 Hz, $W_{1/2}$=12.9 Hz, C*H*OAc), 4.52 and 4.39 (ABdd, 2H, J=12.0 Hz), 3.75-3.93 (m, 2H), 2.03 (s, 3H), 1.90-2.05 (m, 2H), 1.18-1.72 (m, 4H). Anal.Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.61; N, 14.51. Found: C, 62.55; H, 6.79; N, 14.79.

The crude reaction mixture (0.120 g) from the cis epoxide **7** was purified by semipreparative TLC (a 7: 3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-4-azido-*c*-2-benzyloxytetrahydropyran-*r*-3-ol (29)** (0.090 g), as a liquid: IR, see Table 3; ^{1}H NMR (CDCl$_3$) δ 7.18-7.35 (m, 5H), 4.88 (d, 1H, J=3.6 Hz, H$_3$), 4.69 and 4.44 (ABdd, 2H, J=11.6 Hz), 3.72 (ddd, 1H, J=11.9 and 2.5 Hz), 3.53-3.63 (m, 2H), 3.39-3.52 (m, 1H), 1.85 (dquintet, 1H, J=13.3, 4.6 and 2.3 Hz), 1.46-1.58 (m, 1H). Anal.Calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.06; N, 16.85. Found: C, 57.64; H, 5.94; N, 16.71. **Acetate**, a liquid: ^{1}H NMR (CDCl$_3$) δ 7.19-7.48 (m, 5H), 4.97 (d, 1H, J=3.5 Hz, C*H*OBn), 4.66 and 4.43 (ABdd, 2H, J=12.3 Hz), 4.64 (dd, 1H, J=10.2 and 3.4 Hz, $W_{1/2}$=19.6 Hz, C*H*OAc), 3.83-4.01 (m, 1H, $W_{1/2}$=20.0 Hz, CHN), 3.74 (dd, 1H, J=12.1 and 2.4 Hz), 3.58 (ddd, 1H, J=11.6, 5.4 and 1.6 Hz), 2.03 (s, 3H), 1.88-2.02 (m, 1H), 1.66 (ddd, 1H, J=12.6 and 5.4 Hz). Anal.Calcd for $C_{14}H_{17}N_3O_4$: C, 57.72; H, 5.88; N, 14.41. Found: C, 57.54; H, 6.10; 14.70.

The crude reaction product (0.118 g) from the trans epoxide **6** was subjected to semipreparative TLC (a 7: 3 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **43**) afforded pure azido alcohols **43** (0.075 g) and **44** (0.012 g).

***t*-2-Azido-*t*-6-benzyloxy-*r*-1-cyclohexanol (43)**, a liquid: IR, see Table 3; ^{1}H NMR (CDCl$_3$) δ 7.24-7.39 (m, 5H), 4.68 and 4.52 (ABdd, 2H, J=11.3 Hz), 3.40 (unresolved triplet, 1H, J=9.1 Hz, H$_2$), 3.19-3.31 (m, 2H), 2.05-2.19 (m, 1H), 1.89-2.02 (m, 1H), 1.72-1.84 (m, 1H), 1.15-1.41 (m, 3H).

Anal.Calcd for $C_{13}H_{17}N_3O_2$: C, 63.14; H, 6.92; N, 16.98. Found: C, 63.23; H, 6.77; N, 17.24. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.23-7.43 (m, 5H), 4.93 (unresolved triplet, 1H, *J*=9.7 Hz, $W_{1/2}$=19.5 Hz, C*H*OAc), 4.63 and 4.49 (ABdd, 2H, *J*=11.5 Hz), 3.25-3.40 (m, 2H), 2.09 (s, 3H), 1.95-2.21 (m, 2H), 1.72-1.90 (m, 2H), 1.23-1.51 (m, 2H). Anal.Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.61; N, 14.51. Found: C, 62.51; H, 6.73; N, 14.05.

***t*-2-Azido-*t*-3-benzyloxy-*r*-1-cyclohexanol** (**44**), a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.26-7.40 (m, 5H), 4.60 and 4.55 (ABdd, 2H, *J*=11.7 Hz), 3.90-4.08 (m, 2H), 3.17 (dd, 1H, *J*=9.8 and 2.9 Hz, H_2), 1.19-2.12 (m, 6H). Anal.Calcd for $C_{13}H_{17}N_3O_2$: C, 63.14; H, 6.92; N, 16.98. Found: C, 63.29; H, 6.66; N, 16.81. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.15-7.36 (m, 5H), 5.17 (ddd, 1H, *J*=9.0 and 4.2 Hz, $W_{1/2}$=19.6 Hz, C*H*OAc), 4.58 and 4.59 (ABdd, 2H, *J*=11.9 Hz), 3.84-3.95 (m, 1H, $W_{1/2}$=9.8 Hz, C*H*OBn), 3.41 (dd, 1H, *J*=9.0 and 4.0 Hz, $W_{1/2}$=17.6 Hz, CHN), 2.07 (s, 3H), 1.26-2.18 (m, 6H). Anal.Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.61; N, 14.51. Found: C, 62.15; H, 6.43; N, 14.29.

The crude reaction mixture (0.118 g) from the trans epoxide **8** was purified by semipreparative TLC (a 7: 3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-4-azido-*t*-2-benzyloxytetrahydropyran-*r*-3-ol** (**53**) (0.085 g), as a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.16-7.29 (m, 5H), 4.82 and 4.50 (ABdd, 2H, *J*=11.6 Hz), 4.17 (d, 1H, *J*=7.2 Hz, H_3), 3.90 (ddd, 1H, *J*=12.1, 4.9 and 1.8 Hz), 3.28-3.42 (m, 3H), 1.82 (dquintet, 1H, *J*=13.4, 4.6 and 2.2 Hz), 1.48-1.68 (m, 1H). Anal.Calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.06; N, 16.85. Found: C, 57.71; H, 6.15; N, 17.10. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.18-7.33 (m, 5H), 4.81 (dd, 1H, *J*=6.7 and 2.3 Hz, $W_{1/2}$=9.8 Hz, C*H*OAc), 4.78 and 4.52 (ABdd, 2H, *J*=12.2 Hz), 4.32 (d, 1H, *J*=6.8 Hz, C*H*OBn), 3.92-4.02 (m, 1H), 3.33-3.55 (m, 2H), 1.88-2.03 (m, 1H), 2.01 (s, 3H), 1.57-1.77 (m, 1H). Anal.Calcd for $C_{14}H_{17}N_3O_4$: C, 57.72; H, 5.88; N, 14.41. Found: C, 57.41; H, 5.63; N, 14.09.

Azidolysis of Epoxides 5-8 with NaN_3-$LiClO_4$ in CH_3CN. General procedure. A solution of the epoxide (0.50 mmol) in CH_3CN (2 ml) was treated with NaN_3 (0.040 g, 0.61 mmol) and $LiClO_4$ (1.06 g, 10.0 mmol) and the resulting reaction mixture was stirred at 80°C for 18 h. After cooling, dilution with ether and evaporation of the washed (water) organic solution afforded a crude reaction product which was analyzed by GC and ^{1}H NMR to give the results shown in Tables 1 and 2. In the case of cis epoxide **5**, the azidolysis was repeated also in the presence of $Mg(ClO_4)_2$, and $Zn(OSO_2CF_3)_2$ to give the results shown in Table 1.

Azidolysis of cis Epoxides 5 and 7 with LiN_3. The following procedure is typical. A solution of the cis epoxide **5** (0.102 g, 0.50 mmol) in CH_3CN (2.0 ml) was treated with LiN_3 (0.245 g, 5.0 mmol) and the resulting reaction mixture was stirred at 80°C for 72 h. Dilution with ether and evaporation of the washed (water) organic solvent afforded a crude reaction product (0.115 g) consisting of a 83:17 mixture of the two azido alcohols **19** and **20** (GC) which was subjected to semipreparative TLC (a 7: 3 : 0.1 mixture of petroleum ether, AcOEt and MeOH was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **19**) afforded pure **19** (0.078 g) and ***t*-2-azido-*c*-3-benzyloxy-*r*-1-cyclohexanol** (**20**) (0.012 g), as a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.18-7.33 (m, 5H), 4.61 and 4.53 (ABdd, 2H, *J*=11.5 Hz), 3.12-3.35 (m, 3H), 1.82-2.12 (m, 2H), 1.62-1.74 (m, 1H), 1.04-1.38 (m, 3H). Anal.Calcd for $C_{13}H_{17}N_3O_2$: C, 63.14; H, 6.92; N, 16.98. Found: C, 63.37; H, 6.81; N, 17.15. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.26-7.44 (m, 5H), 4.66 (s, 2H), 4.50-4.62 (m, 1H, $W_{1/2}$=18.5 Hz, C*H*OAc), 3.41 (unresolved triplet, 1H, *J*=9.6 Hz, $W_{1/2}$=19.0 Hz, CHN), 3.21-3.38 (m, 1H, $W_{1/2}$=20.0 Hz, C*H*OBn), 2.01 (s, 3H), 1.95-2.20 (m, 2H), 2.10 (s, 3H), 1.52-1.82 (m, 2H), 1.10-1.38 (m, 2H). Anal.Calcd for $C_{15}H_{19}N_3O_3$: C, 62.27; H, 6.61; N, 14.51. Found: C, 62.01; H, 6.94; N, 14.26.

The crude reaction product from the cis epoxide **7** (0.120 g) was subjected to semipreparative TLC (a 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **29**) afforded pure **29** (0.079 g) and ***c*-2-benzyloxy-*t*-3-azidotetrahydropyran-*r*-4-ol** (**30**) (0.015 g) as a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.19-7.34 (m, 5H), 4.83 and 4.63 (ABdd, 2H, *J*=11.7 Hz), 4.28 (d, 1H, *J*=7.1 Hz, H_3), 3.87-4.12 (m, 1H), 3.40-3.53 (m, 2H), 3.20 (dd, 1H, *J*=8.7 and 7.1 Hz, H_2), 1.84-1.95 (m, 1H), 1.57-1.76 (m, 1H). Anal.Calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.06; N, 16.85. Found: C, 57.71; H, 6.15; N, 16.74. **Acetate**, a solid, m.p. 100-101°C: ^{1}H NMR ($CDCl_3$) δ 7.26-7.39 (m, 5H), 4.91 and 4.68 (ABdd, 2H, *J*=11.7 Hz), 4.71 (ddd, 1H, *J*=10.0 and 5.2 Hz, $W_{1/2}$=28.0 Hz, C*H*OAc), 4.31 (d, 1H, *J*=7.7 Hz, C*H*OBn), 4.01 (ddd, 1H, *J*=12.2, 5.0 and 1.9 Hz), 3.35-3.50 (m, 2H), 2.10 (s, 3H), 1.97-2.15 (m, 1H), 1.57-1.80 (m, 1H). Anal.Calcd for $C_{14}H_{17}N_3O_4$: C, 57.72; H, 5.88; N, 14.41. Found: C, 57.41; H, 5.63; N, 14.62.

Aminolysis of Epoxides 5-8 with $NHEt_2$ in EtOH. The following procedure is typical. A solution of the cis epoxide **5** (0.102 g, 0.50 mmol) in EtOH (1.0 ml) containing $NHEt_2$ (0.14 ml, 1.26 mmol) was stirred at 80°C for 3 days. After cooling, dilution with ether and evaporation of the washed (water) organic solution afforded a crude reaction product (0.110 g), consisting of the amino alcohol **21** and the unreacted epoxide **5** (52%) (^1H NMR, see Table 1) which was subjected to semipreparative TLC (a 7: 3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense slower moving band afforded pure ***c*-2-benzyloxy-*t*-6-(*N*,*N*-diethylamino)-*r*-1-cyclohexanol (21)** (0.050 g), as a liquid: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.19-7.41 (m, 5H), 4.81 and 4.64 (ABdd, 2H, J= 12.3 Hz), 3.93-4.06 (m, 1H, H_3), 3.39 (dd, 1H, J= 10.5 and 2.7 Hz, H_2), 3.03 (ddd, 1H, J=11.6 and 3.2 Hz, H_1), 2.60 (sextet, 2H, J=7.3 Hz), 2.40 (sextet, 2H, J=6.8 Hz), 1.47-1.92 (m, 4H), 1.05 (t, 6H, J=7.2 Hz), 0.94-1.32 (m, 2H). Anal.Calcd for $C_{17}H_{27}NO_2$: C, 73.60; H, 9.81; N, 5.04. Found: C, 73.51; H, 9.84; N, 5.31. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.14-7.30 (m, 5H), 4.80 (dd, 1H, J=10.4 and 2.9 Hz, $W_{1/2}$=15.3, C*H*OAc), 4.50 (s, 2H), 3.74-3.84 (m, 1H, $W_{1/2}$=9.5 Hz, C*H*OBn), 3.05 (ddd, 1H, J= 11.0 and 3.8 Hz, $W_{1/2}$=26.0 Hz, CHN), 2.26-2.58 (m, 5H), 1.97 (s, 3H), 1.08-1.91 (m, 6H), 0.89 (t, 6H, J=7.0 Hz). Anal.Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.46; H, 9.37; N, 4.44.

The crude reaction product (0.122 g) from the cis epoxide **7** was purified by semipreparative TLC (a 75:25 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-2-benzyloxy-*t*-4-(*N*,*N*-diethylamino)tetrahydropyran-*r*-3-ol (31)** (0.090 g), as a solid m.p. 147-148°C: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.23-7.43 (m, 5H), 5.09 (d, 1H, J=3.5 Hz, H_3), 4.77 and 4.61 (ABdd, 2H, J=12.5 Hz), 3.58-3.81 (m, 2H), 3.53 (dd, 1H, J=8.1 and 4.4 Hz, H_2), 3.09-3.22 (m, 1H, H_1), 2.60-2.78 (m, 2H), 2.37-2.54 (sextet, 2H, J=6.9 Hz), 1.61-1.73 (m, 2H), 1.07 (t, 6H, J=7.2 Hz). Anal.Calcd for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.01; N, 5.01. Found: C, 68.49; H, 9.19; N, 5.24. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.27-7.35 (m, 5H), 4.90-4.98 (m, 2H), 4.76 and 4.51 (ABdd, 2H, J=12.4 Hz), 3.85 (ddd, 1H, J=11.8 and 2.7 Hz), 3.49-3.72 (m, 2H), 2.71 (q, 4H, J=7.2 Hz), 2.06 (s, 3H), 1.72-2.20 (m, 2H), 1.14 (t, 6H, J=7.2 Hz). Anal.Calcd for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.46; N, 4.35. Found: C, 67.01; H, 8.12; N, 4.14.

The crude reaction product (0.125 g) from the trans epoxide **6** was purified by semipreparative TLC (an 8:2 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-benzyloxy-*t*-6-(*N*,*N*-diethylamino)-*r*-1-cyclohexanol (45)** (0.095 g), as a liquid: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.18-7.42 (m, 5H), 4.81 and 4.71 (ABdd, 2H, J=12.0 Hz), 3.24-3.42 (m, 2H), 3.12-3.23 (m, 1H, H_1), 2.65 (sextet, 2H, J=7.2 Hz), 2.38 (sextet, 2H, J=6.8 Hz), 1.91-2.12 (m, 2H), 1.61-1.88 (m, 2H), 1.10-1.41 (m, 2H), 1.04 (t, 6H, J=7.0 Hz). Anal.Calcd for $C_{17}H_{27}NO_2$: C, 73.60; H, 9.81; N, 5.04. Found: C, 73.41; H, 9.62; N, 5.09. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.17-7.30 (m, 5H), 4.85 (dd, 1H, J=10.4 and 9.1 Hz, $W_{1/2}$= 19.2 Hz, C*H*OAc), 4.56 and 4.46 (ABdd, 2H, J=12.2 Hz), 3.21-3.33 (m, 1H, $W_{1/2}$=20.0 Hz, C*H*OBn), 2.36-2.59 (m, 3H), 2.28 (sextet, 1H, J=6.7 Hz), 1.96 (s, 3H), 1.88-2.10 (m, 2H), 1.62-1.78 (m, 2H), 1.05-1.30 (m, 2H), 0.87 (t, 6H, J=7.0 Hz). Anal.Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.70; H, 9.33; N, 4.64.

The crude reaction product (0.128 g) from the trans epoxide **8** was purified by preparative TLC (an 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-benzyloxy-*t*-4-(*N*,*N*-diethylamino)tetrahydropyran-*r*-3-ol (55)** (0.104 g), a liquid; IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.18-7.37 (m, 5H), 4.83 and 4.62 (ABdd, 2H, J=11.8 Hz), 4.25 (d, 1H, J=7.3 Hz, H_3), 3.93-4.02 (m, 1H, H_2), 3.23-3.41 (m, 3H), 2.52-2.70 (m, 3H), 2.24-2.41 (sextet, 2H, J=6.8 Hz), 1.56-1.62 (m, 2H), 0.98 (t, 3H, J=7.0 Hz). Anal.Calcd for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.01; N, 5.01. Found: C, 69.05; H, 9.29; N, 5.33. **Acetate**, a liquid; ^1H NMR ($CDCl_3$) δ 7.19-7.30 (m, 5H), 4.78 and 4.54 (ABdd, 2H, J=12.5 Hz), 4.82 (dd, 1H, J=7.6 and 2.8 Hz, $W_{1/2}$=18.0 Hz, C*H*OAc), 4.25 (d, 1H, J=7.6 Hz, C*H*OBn), 3.94 (dt, 1H, J=10.7 and 3.3 Hz), 3.22-3.35 (m, 1H), 2.60-2.75 (m, 1H, $W_{1/2}$=19.0 Hz, CHN), 2.37-2.73 (m, 2H), 2.20-2.33 (m, 2H), 1.95 (s, 3H), 1.55-1.67 (m, 2H). Anal.Calcd for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.46; N, 4.35. Found: C, 67.34; H, 8.21; N, 4.17.

Reaction of Epoxides 5-8 with $NHEt_2$-$LiClO_4$ in CH_3CN. The following procedure is typical. A solution of the cis epoxide **5** (0.102 g, 0.50 mmol) in anhydrous CH_3CN (4.0 ml) was treated with $NHEt_2$ (0.14 ml, 1.26 mmol) and $LiClO_4$ (2.12 g, 20.0 mmol) and the resulting reaction mixture was stirred at 80°C for 18 h. After cooling, dilution with ether, and evaporation of the washed (water) organic solution afforded a crude reaction product (0.128 g) consisting of a 60:40 mixture of amino alcohols **21** and **22** (^1H NMR, Table 1) which was subjected to semipreparative TLC (a 6:3:1 mixture of petroleum ether, AcOEt, and

NEt_3 was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **22**) afforded pure **21** (0.065 g) and ***c*-3-benzyloxy-*t*-2-(*N*,*N*-diethylamino)-*r*-1-cyclohexanol (22)** (0.038 g), as a liquid: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.26-7.36 (m, 5H), 4.63 and 4.40 (ABdd, 2H, J=11.3 Hz), 3.42-3.52 (m, 1H, H_3), 3.13-3.23 (m, 1H, H_1), 2.65-2.86 (m, 4H), 2.45 (t, 1H, J=9.9 Hz, H_2), 2.20-2.37 (m, 1H), 2.04-2.19 (m, 1H), 1.67-1.82 (m, 1H), 1.18-1.36 (m, 2H), 1.06 (t, 6H, J=7.0 Hz). Anal.Calcd for $C_{17}H_{27}NO_2$: C, 73.60; H, 9.81; N, 5.04. Found: C, 73.52; H, 9.99; N, 4.91. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.28-7.38 (m, 5H), 4.74 (ddd, 1H, J=10.5 and 5.8 Hz, $W_{1/2}$=19.0 Hz, C*H*OAc), 4.63 and 4.54 (ABdd, 2H, J=11.8 Hz), 3.43 (ddd, 1H, J=10.1 and 5.5 Hz, $W_{1/2}$=19.0 Hz, C*H*OBn), 2.64-2.81 (m, 5H), 2.04 (s, 3H), 1.18-1.42 (m, 6H), 1.00 (t, 6H, J=7.2 Hz). Anal.Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.55; H, 9.11; N, 4.06.

The crude reaction product (0.13 g) from the cis epoxide **7** was subjected to semipreparative TLC (a 75:24:1 mixture of petroleum ether, AcOEt and NEt_3 was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **32**) afforded pure **31** (0.065 g) and ***c*-2-benzyloxy-*t*-3-(*N*,*N*-diethylamino)tetrahydropyran-*r*-4-ol (32)** (0.015 g), as a liquid; IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.19-7.30 (m, 5H), 4.81 and 4.47 (ABdd, 2H, J=11.7 Hz), 4.41 (d, 1H, J=8.5 Hz, H_3), 3.88-3.99 (ddd, 1H, J=12.0, 5.1 and 1.7 Hz), 3.50 (ddd, 1H, J=10.4 and 5.0 Hz, H_1), 3.35 (ddd, 1H, J=12.4 and 2.3 Hz), 2.55-2.79 (m, 4H), 2.44 (dd, 1H, J=10.0 and 8.3 Hz, H_2), 1.91-2.04 (m, 1H), 1.51-1.73 (m, 1H), 0.99 (t, 6H, J=7.0 Hz). Anal.Calcd for $C_{16}H_{25}NO_3$: C, 68.78; H, 9.01; N, 5.01. Found: C, 68.48; H, 8.74; N, 5.18. **Acetate**, a semisolid: ^1H NMR ($CDCl_3$) δ 7.26-7.39 (m, 5H), 5.00 (ddd, 1H, J=10.4 and 5.3 Hz, C*H*OAc), 4.87 and 4.57 (ABdd, 2H, J=11.7 Hz), 4.50 (d, 1H, J=9.3 Hz, C*H*OBn), 3.96 (ddd, 1H, J=12.0, 5.0 and 1.9 Hz), 3.40 (ddd, 1H, J=12.0 and 2.6 Hz), 2.58-2.75 (m, 5H), 2.05 (s, 3H), 1.89-2.13 (m, 1H), 1.65-1.86 (m, 1H). Anal.Calcd for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.46; N, 4.35. Found: C, 67.55; H, 8.63; N, 4.25.

The crude reaction products from the trans epoxides **6** and **8** turned out to be consistent only of the amino alcohols **45** and **55**, respectively.

Reaction of Epoxides 5-8 with PhSH-NEt_3. General Procedure. A solution of the epoxide (0.50 mmol) in MeOH (0.5 ml) was treated with PhSH (0.15 ml, 1.5 mmol) and NEt_3 (0.26 ml, 2.0 mmol).[20] After 24 h at r.t., dilution with ether and evaporation of the washed (saturated aqueous $NaHCO_3$ and water) organic solution afforded a crude reaction product which was analyzed by ^1H NMR (see Tables 1 and 2).

The crude reaction product (0.150 g) from the cis epoxide **5**, essentially consisting of the thioalcohol **23**, was purified by semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-2-benzyloxy-*t*-6-(phenylthio)-*r*-1-cyclohexanol (23)** (0.12 g), as a liquid: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.32-7.43 (m, 2H), 7.08-7.30 (m, 8H), 4.55 and 4.45 (ABdd, 2H, J=12.0 Hz), 3.81 (ddd, 1H, J=6.0 and 2.8 Hz, H_3), 3.52 (dd, 1H, J= 8.3 and 2.7 Hz, H_2), 3.35 (ddd, 1H, J=8.4 and 4.2 Hz, H_1), 1.72-2.06 (m, 2H), 1.22-1.63 (m, 4H). Anal.Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.45; H, 7.23. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.33-7.38 (m, 2H), 7.11-7.30 (m, 8H), 4.89 (dd, 1H, J= 8.6 and 2.6 Hz, $W_{1/2}$=13.0 Hz, C*H*OAc), 4.47 (s, 2H), 3.81 (ddd, 1H, J=6.0 and 2.7 Hz, $W_{1/2}$=13.0 Hz, C*H*OBn), 3.57 (ddd, 1H, J=8.8 and 4.6 Hz, $W_{1/2}$=13.0 Hz, CHS), 1.90 (s, 3H), 1.68-2.01 (m, 2H), 1.28-1.67 (m, 4H). Anal.Calcd for $C_{21}H_{24}O_3S$: C, 70.76; H, 6.78. Found: C, 70.47; H, 7.01.

The crude reaction product (0.143 g) from the cis epoxide **7**, essentially consisting of the thioalcohol **33**, was purified by semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-2-benzyloxy-*t*-4-(phenylthio)tetrahydropyran-*r*-3-ol (33)** (0.112 g), as a solid m.p. 72-73°C: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.37-7.43 (m, 2H), 7.17-7.30 (m, 8H), 4.88 (d, 1H, J=3.3 Hz, H_3), 4.68 and 4.46 (ABdd, 2H, J=11.8 Hz), 3.68 (ddd, 1H, J=11.7 and 2.6 Hz), 3.37-3.52 (m, 2H), 3.26 (ddd, 1H, J=11.2 and 4.1 Hz), 2.34 (m, 1H), 1.80-1.91 (m, 1H), 1.50-1.71 (m, 1H). Anal.Calcd for $C_{18}H_{20}O_3S$: C, 68.33; H, 6.37. Found: C, 68.21; H, 6.45. **Acetate**, a liquid: ^1H NMR ($CDCl_3$) δ 7.28-7.42 (m, 2H), 7.06-7.25 (m, 8H), 4.86 (d, 1H, J=3.4 Hz, C*H*OBn), 4.73 (dd, 1H, J=10.9 and 3.4 Hz, $W_{1/2}$=15.7 Hz, C*H*OAc), 4.64 and 4.41 (ABdd, 2H, J=12.3 Hz), 3.74 (ddd, 1H, J=11.8 and 2.6 Hz), 3.43-3.65 (m, 2H), 1.83-2.05 (m, 1H), 1.86 (s, 3H), 1.70 (ddd, 1H, J=12.1 and 5.1 Hz). Anal.Calcd for $C_{20}H_{22}O_4S$: C, 67.02; H, 6.18. Found: C, 67.15; H, 6.21.

The crude reaction product (0.145 g) from the trans epoxide **6** was subjected to semipreparative TLC (a 5:5:0.1 mixture of benzene, petroleum ether and MeOH was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **47**) afforded pure thioalcohols **47** (0.105 g) and **48** (0.015 g).

***t*-2-Benzyloxy-*t*-6-(phenylthio)-*r*-1-cyclohexanol (47)**, a solid m.p. 50-52°C: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.40-7.45 (m, 2H), 7.18-7.29 (m, 8H), 4.62 and 4.56 (ABdd, 2H, *J*=11.7 Hz), 3.22-3.48 (m, 2H), 2.72-2.90 (m, 1H, H_1), 1.85-2.10 (m, 2H), 1.48-1.75 (m, 2H), 1.03-1.38 (m, 2H). Anal.Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.23; H, 7.41. **Acetate**, a solid m.p. 105-106°C: ^{1}H NMR ($CDCl_3$) δ 7.36-7.41 (m, 2H), 7.15-7.29 (m, 8H), 4.91 (dd, 1H, *J*=10.6 and 9.1 Hz, $W_{1/2}$=19.6 Hz, C*H*OAc), 4.53-4.43 (ABdd, 2H, *J*=12.1 Hz), 3.20-3.38 (m, 1H, $W_{1/2}$=19.6 Hz, C*H*OBn), 2.85-3.03 (m, 1H, $W_{1/2}$=23.5 Hz, CHS), 1.47-2.12 (m, 4H), 1.85 (s, 3H), 1.03-1.40 (m, 2H). Anal.Calcd for $C_{21}H_{24}O_3S$: C, 70.76; H, 6.78. Found: C, 70.71; H, 6.94.

***t*-3-Benzyloxy-*t*-2-(phenylthio)-*r*-1-cyclohexanol (48)**, a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.09-7.42 (m, 10H), 4.54 and 4.47 (ABdd, 2H, *J*=11.4 Hz), 3.90-4.01 (m, 1H, H_3), 3.85 (dd, 1H, *J*=10.3 and 4.5 Hz, H_1), 2.97 (dd, 1H, *J*=10.1 and 2.9 Hz, H_2), 1.85-2.16 (m, 2H), 1.42-1.80 (m, 2H), 1.12-1.40 (m, 2H). Anal.Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.26; H, 7.12. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.38-7.42 (m, 2H), 7.08-7.29 (m, 8H), 5.13 (ddd, 1H, *J*=8.4 and 4.0 Hz, $W_{1/2}$=21.6 Hz, C*H*OAc), 4.48 (s, 2H), 3.92 (ddd, 1H, *J*=6.2 and 2.8 Hz, $W_{1/2}$=13.0 Hz, C*H*OBn), 3.36 (dd, 1H, *J*=8.3 and 3.2 Hz, $W_{1/2}$=13.0 Hz, CHS), 1.81-2.06 (m, 2H), 1.18 (s, 3H), 1.25-1.75 (m, 4H). Anal.Calcd for $C_{21}H_{24}O_3S$: C, 70.76; H, 6.78. Found: C, 70.82; H, 6.53.

The crude reaction product (0.142 g) from the trans epoxide **8**, essentially consisting of the thioalcohol **57**, was purified by semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-benzyloxy-*t*-4-(phenylthio)tetrahydropyran-*r*-3-ol (57)** (0.115 g), as a solid, mp 66-67°C: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.46-7.53 (m, 2H), 7.18-7.38 (m, 8H), 4.88 and 4.62 (ABdd, 2H, *J*=11.7 Hz), 4.32 (d, 1H, *J*=7.1 Hz, H_3), 3.96 (ddd, 1H, *J*=11.9, 4.6 and 1.9 Hz), 3.44 (ddd, 1H, *J*=11.8 and 2.5 Hz), 3.28-3.39 (m, 1H, H_1), 2.93-3.00 (m, 1H, H_2), 1.93 (dquintet, 1H, *J*=11.4, 4.5 and 2.2 Hz), 1.63-1.82 (m, 1H). Anal.Calcd for $C_{18}H_{20}O_3S$: C, 68.33; H, 6.37. Found: C, 68.09; H, 6.21. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.36-7.43 (m, 2H), 7.12-7.32 (m, 8H), 4.84 (dd, 1H, *J*=9.1 and 6.4 Hz, C*H*OAc), 4.76 and 4.48 (ABdd, 2H, *J*=11.0 Hz), 4.32 (d, 1H, *J*=6.4 Hz, C*H*OBn), 3.95 (dt, 1H, *J*=11.4 and 3.7 Hz), 3.31-3.45 (m, 1H), 3.04-3.18 (ddd, 1H, *J*=10.6, 8.4 and 4.2 Hz, $W_{1/2}$=23.4 Hz, CHS), 1.92-2.03 (m, 1H), 1.87 (s, 3H), 1.51-1.69 (m, 1H). Anal.Calcd for $C_{20}H_{22}O_4S$: C, 67.02; H, 6.18. Found: C, 67.11; H, 6.32.

Reaction of Epoxides 5-8 with PhSH-$LiClO_4$ in CH_3CN. General procedure. A solution of the epoxide (0.50 mmol) in anhydrous CH_3CN (1.0 ml) was treated with PhSH (0.08 ml, 0.74 mmol) and $LiClO_4$ (0.265 g, 2.5 mmol) and the reaction mixture was stirred at 80°C for 18 h. Usual workup afforded a crude reaction product which was analyzed by ^{1}H NMR to give the results shown in Tables 1 and 2.

The crude reaction product (0.152 g) from the cis epoxide **5** was subjected to semipreparative TLC (a 5:5:0.1 mixture of benzene, petroleum ether and MeOH was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **23**) afforded pure thioalcohol **23** (0.055 g) and ***c*-3-benzyloxy-*t*-2-(phenylthio)-*r*-1-cyclohexanol (24)** (0.065 g), as a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.40-7.53 (m, 2H), 7.22-7.35 (m, 8H), 4.64 and 4.56 (ABdd, 2H, *J*=11.4 Hz), 3.45-3.61 (m, 1H, H_1), 3.39 (ddd, 1H, *J*=8.5 and 3.9 Hz, H_3), 3.07 (unresolved triplet, 1H, *J*=8.0 Hz, H_2), 1.96-2.21 (m, 2H), 1.65-1.92 (m, 2H), 1.15-1.58 (m, 2H). Anal.Calcd for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.61; H, 7.33. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.36-7.45 (m, 2H), 7.09-7.31 (m, 8H), 4.74 (ddd, 1H, *J*=9.8 and 4.5 Hz, $W_{1/2}$=20.2 Hz, C*H*OAc), 4.57 and 4.56 (ABdd, 2H, *J*=11.5 Hz), 3.24 (ddd, 1H, *J*=9.5 and 4.3 Hz, $W_{1/2}$=20.2 Hz, C*H*OBn), 3.08 (t, 1H, *J*=9.6 Hz, $W_{1/2}$=20.6 Hz, CHS), 1.89-2.18 (m, 2H), 1.55-1.80 (m, 2H), 1.10-1.44 (m, 2H), 1.85 (s, 3H). Anal.Calcd for $C_{21}H_{24}O_3S$: C, 70.76; H, 6.78. Found: C, 70.50; H, 6.72.

The crude reaction product (0.150 g) from the cis epoxide **7** was subjected to semipreparative TLC (an 8:2 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **33**) afforded pure **33** (0.095 g) and ***c*-2-benzyloxy-*t*-3-(phenylthio)tetrahydropyran-*r*-4-ol (34)** (0.023 g), as a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.15-7.37 (m, 10H), 4.75 and 4.50 (ABdd, 2H, *J*=11.8 Hz), 4.60 (d, 1H, *J*=4.9 Hz, H_3), 3.97-4.07 (m, 1H), 3.68-3.80 (m, 1H, H_1), 3.39-3.53 (m, 1H), 3.09 (unresolved triplet, 1H, *J*=5.7 Hz, H_2), 2.11-2.21

(m, 1H), 1.53-1.69 (m, 1H). Anal.Calcd for $C_{18}H_{20}O_3S$: C, 68.33; H, 6.37. Found: C, 68.01; H, 6.05. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.34-7.40 (m, 2H), 7.13-7.28 (m, 8H), 4.86 (ddd, 1H, *J*=8.1 and 4.1 Hz, $W_{1/2}$=19.1 Hz, C*H*OAc), 4.77 and 4.49 (ABdd, 2H, *J*=11.8 Hz), 4.51 (d, 1H, *J*=6.1 Hz, C*H*OBn), 3.95-4.06 (m, 1H), 3.36-3.48 (eight lines, 1H, *J*=11.7, 8.6 and 3.1 Hz), 3.20 (dd, 1H, *J*=7.9 and 6.0 Hz, $W_{1/2}$=15.0 Hz, CHS), 2.04-2.16 (m, 1H), 1.94 (s, 3H), 1.48-1.70 (m, 1H). Anal.Calcd for $C_{20}H_{22}O_4S$: C, 67.02; H, 6.18. Found: C, 66.89; H, 6.00.

The crude reaction products from the trans epoxides **6** and **8** were analyzed by ^{1}H NMR to give the results as shown in Table 2.

Reaction of Epoxides 5 and 6 with Me_2CuLi. The following procedure is typical. 1.6 M MeLi in ether (3.75 ml) was added at -15°C to a suspension of CuI (0.57 g, 3.0 mmol) in anhydrous ether (5 ml). After 15 min at the same temperature, a solution of the cis epoxide **5** (0.204 g, 1.0 mmol) in anhydrous ether (5 ml) was added and, after 30 min, the reaction mixture was slowly (4 h) warmed to 0°C. After 1 h at 0°C (24 h at r.t. in the case of the trans epoxide **6**), ether and saturated aqueous NH_4Cl were added. Evaporation of the separated and washed (water) organic solution afforded a crude reaction product (0.218 g) (Table 1) which was subjected to preparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **25**) afforded pure methyl alcohols **25** (0.13 g) and **26** (0.050 g).

***c*-2-Benzyloxy-*t*-6-methyl-*r*-1-cyclohexanol (25)**, a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.15-7.29 (m, 5H), 4.58 and 4.33 (ABdd, 2H, *J*=11.6 Hz), 3.62-3.72 (m, 1H, H_3), 2.95-3.13 (m, 1H, H_2), 1.91-2.20 (m, 2H), 1.10-1.78 (m, 5H), 0.90 (d, 3H, *J*=6.6 Hz). Anal.Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.44; H, 9.06.

***c*-3-Benzyloxy-*t*-2-methyl-*r*-1-cyclohexanol (26)**, a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.15-7.30 (m, 5H), 4.56 and 4.37 (ABdd, 2H, *J*=11.6 Hz), 3.23 (ddd, 1H, *J*=8.4 and 3.5 Hz, H_3), 3.03 (ddd, 1H, *J*=8.6 and 3.6 Hz, H_1), 1.51-2.01 (m, 3H), 1.16-1.41 (m, 4H), 1.04 (d, 3H, *J*=6.7 Hz). Anal.Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.34; H, 9.42.

The crude reaction product (0.21 g) from the trans epoxide **6** was subjected to semipreparative TLC (a 85:15 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **49**) afforded pure methyl alcohols **49** (0.095 g) and **50** (0.0.52 g).

***t*-2-benzyloxy-*t*-6-methyl-*r*-1-cyclohexanol (49)**, a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.16-7.30 (m, 5H), 4.61 and 4.40 (ABdd, 2H, *J*=11.5 Hz), 3.10-3.18 (m, 1H, H_3), 3.00 (t, 1H, *J*=9.5 Hz, H_2), 0.97 (d, 3H, *J*=6.3 Hz), 2.02-2.10 (m, 1H), 1.12-1.72 (m, 6H). Anal.Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.14; H, 8.96.

***t*-3-benzyloxy-*t*-2-methyl-*r*-1-cyclohexanol (50)**, a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.24-7.35 (m, 5H), 4.57 and 4.37 (ABdd, 2H, *J*=11.9 Hz), 3.69 (ddd, 1H, *J*=9.4 and 4.1 Hz, H_1), 3.64 (m, 1H, H_3), 1.87-2.13 (m, 2H), 1.47-1.80 (m, 3H), 1.18-1.42 (m, 2H), 1.10 (d, 3H, *J*=6.8 Hz). Anal.Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.09; H, 9.01.

Reaction of Epoxides 5-8 with $AlMe_3$. The following procedure is typical. A solution of the cis epoxide **5** (0.102 g, 0.50 mmol) in anhydrous pentane (5.0 ml) was treated at -50°C with 2M $AlMe_3$ in hexane (0.6 ml). The reaction mixture was stirred at the same temperature for 20 min, then slowly warmed to 0°C, stirred 5 h at this temperature, then 18 h at r.t. Dilution with ether (30 ml), followed by carefull addition of water and 5% aqueous HCl, and evaporation of the washed (saturated aqueous $NaHCO_3$ and water) ether solution afforded a crude liquid product (0.101 g) consisting of an 84:16 mixture of methyl alcohols **25** and **26** (GC and ^{1}H NMR).

The crude reaction product (0.106 g) from the cis epoxide **7** was subjected to semipreparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-2-benzyloxyy-*t*-4-methyltetrahydropyran-*r*-3-ol (35)**, as a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.17-7.28 (m, 5H), 4.78 (d, 1H, *J*=3.5 Hz, H_3), 4.71 and 4.40 (ABdd, 2H, *J*=11.6 Hz), 3.69 (ddd, 1H, *J*=11.3 and 2.6 Hz), 3.45 (dq, 1H, *J*=11.2, 4.9 and 1.5 Hz), 3.07 (m, 1H, H_2), 1.67-1.84 (m, 1H), 1.50-1.57 (m, 1H), 1.22-1.41 (m, 1H), 0.95 (d, 3H, *J*=6.4 Hz). Anal.Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.04; H, 8.25. **Acetate**, a liquid; ^{1}H NMR ($CDCl_3$) δ 7.15-7.28 (m, 5H), 4.85 (d, 1H, *J*=3.4 Hz, C*H*OBn), 4.67 and 4.47 (ABdd, 2H, *J*=12.1 Hz), 4.45 (d, 1H, *J*=11.1 Hz, C*H*OAc), 3.76 (ddd, 1H, *J*=11.6 and 2.6 Hz), 3.48 (ddd, 1H, *J*=11.2, 5.0 and 1.4 Hz), 2.01-2.22 (m, 1H), 1.98 (s, 3H), 1.56-

1.71 (m, 1H), 1.45 (ddd, 1H, *J*=12.2 and 5.0 Hz), 0.85 (d, 3H, *J*=6.4 Hz). Anal.Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.62. Found: C, 68.31; H, 7.98.

The crude reaction product from the trans epoxide **6** gave the result shown in Table 2.

The crude reaction product (0.102 g) from the trans epoxide **8** was subjected to semipreparative TLC (a 9:1 mixture of petroleum ether and AcOEt was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-benzyloxy-*t*-4-methyltetrahydropyran-*r*-3-ol (59)** (0.080 g), as a solid m.p. 74-76°C: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.24-7.30 (m, 5H), 4.89 and 4.57 (ABdd, 2H, *J*=11.6 Hz), 4.21 (d, 1H, *J*=7.4 Hz, H_3), 3.94 (dq, 1H, *J*=11.7, 4.7, and 1.4 Hz), 3.46 (ddd, 1H, *J*=11.8 and 2.5 Hz), 3.04 (dd, 1H, *J*=9.5 and 7.5 Hz, H_2), 1.51-1.67 (m, 2H), 1.36-1.49 (m, 1H), 1.05 (d, 3H, *J*=6.0 Hz). Anal.Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.41; H, 8.13. **Acetate**, a liquid: ^{1}H NMR ($CDCl_3$) δ 7.12-7.31 (m, 5H), 4.77 and 4.51 (ABdd, 2H, *J*=12.5 Hz), 4.53 (t, 1H, *J*=7.5 Hz, $W_{1/2}$=15.0 Hz, C*H*OAc), 4.29 (d, 1H, *J*=6.9 Hz, C*H*OBn), 3.91 (dt, 1H, *J*=11.6 and 2.9 Hz), 3.40 (ddd, 1H, *J*=11.3 and 2.5 Hz), 1.98 (s, 3H), 1.58-1.79 (m, 1H), 1.36-1.51 (m, 1H), 0.91 (d, 3H, *J*=6.4 Hz). Anal.Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.62. Found: C, 68.39; H, 7.31.

Reaction of Epoxides 5-8 with $AlMe_3$ in the Presence of 12-Crown-4. General procedure. A solution of $AlMe_3$ (1.5 mmol) in pentane (3 ml) was treated at 0°C, under nitrogen, with 12-crown-4 (0.25 ml, 1.6 mmol) and the resulting reaction suspension was stirred at r.t. for 15 h. The epoxide (0.5 mmol) in pentane (2 ml) was added and the reaction mixture was stirred for 18 h at r.t. Usual workup afforded a crude reaction product which was analyzed by GC and ^{1}H NMR to give the results shown in Tables 1 and 2.

Reaction of Epoxides 5-8 with $LiAlH_4$. General procedure. A solution of the epoxide (0.5 mmol) in pentane (5 ml) was treated with $LiAlH_4$ (0.10 g) and the resulting suspension was stirred 4 h at r.t. Usual workup afforded a crude reaction product which was analyzed by GC and ^{1}H NMR to give the results shown in Tables 1 and 2.

The crude reaction product (0.10 g) from the cis epoxide **5** was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **27**) afforded pure alcohols **27** (0.055 g) and **28** (0.025 g).

cis-2-Benzyloxy-1-cyclohexanol (27), a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.15-7.35 (m, 5H), 4.52 and 4.43 (ABdd, 2H, *J*=11.8 Hz), 3.70-3.87 (m, 1H, H_3), 3.38-3.50 (m, 1H, H_2), 1.62-1.87 (m, 2H), 1.32-1.63 (m, 4H), 1.07-1.30 (m, 2H). Anal.Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.74; H, 8.57.

cis-3-Benzyloxy-1-cyclohexanol (28), a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.14-7.34 (m, 5H), 4.48 and 4.45 (ABdd, 2H, *J*=11.8 Hz), 3.57-3.72 (seven lines, 1H, *J*=8.0 and 3.4 Hz, H_3), 3.40-3.51 (seven lines, 1H, *J*=7.3 and 3.7 Hz, H_1), 1.92-2.10 (m, 1H), 1.10-1.89 (m, 7H). Anal.Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.81; H, 8.69.

The crude reaction product (0.101 g) from the cis epoxide **7** was subjected to semipreparative TLC (a 7:3:0.1 mixture of petroleum ether, ether and MeOH was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **37**) afforded pure alcohol **38** (0.015 g)^1 and **cis-2-benzyloxytetrahydropyran-3-ol (37)** (0.069 g), as a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.26-7.38 (m, 5H), 4.81 and 4.53 (ABdd, 2H, *J*=11.7 Hz), 4.82 (d, 1H, *J*=3.2 Hz, H_3), 3.66-3.80 (m, 2H), 3.48-3.57 (m, 1H), 1.55-1.90 (m, 4H). Anal.Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.48; H, 7.65.

The crude reaction product (0.101 g) from the trans epoxide **6** was subjected to semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **51**) afforded pure alcohols **51** (0.055 g) and **52** (0.024 g).

trans-2-Benzyloxy-1-cyclohexanol (51), a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.15-7.28 (m, 5H), 4.60 and 4.38 (ABdd, 2H, *J*=11.6 Hz), 3.34-3.55 (m, 1H, H_3), 3.06-3.22 (m, 1H, H_2), 1.85-2.15 (m, 2H), 1.45-1.80 (m, 2H), 1.04-1.38 (m, 4H). Anal.Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.53; H, 8.61.

trans-3-Benzyloxy-1-cyclohexanol (52), a liquid: IR, see Table 3; ^{1}H NMR ($CDCl_3$) δ 7.14-7.28 (m, 5H), 4.45 and 4.44 (ABdd, 2H, *J*=12.0 Hz), 4.00 (seven lines, 1H, *J*=7.8 and 3.7 Hz, H_3), 3.68-3.80

(m, 1H, H_1), 1.80-1.98 (m, 1H), 1.45-1.82 (m, 7H). Anal.Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.94; H, 8.83.

The crude reaction product (0.102 g) from the trans epoxide **8**, essentialy consisting of the alcohol **61** was purified by semipreparative TLC (a 7:3 mixture of petroleum ether and ether was used as the eluant). Extraction of the most intense band afforded pure **trans-2-benzyloxytetrahydropyran-3-ol (61)** (0.090 g), as a liquid: IR, see Table 3; ^1H NMR ($CDCl_3$) δ 7.19-7.31 (m, 5H), 4.78 and 4.48 (ABdd, 2H, *J*=11.7 Hz), 4.30 (d, 1H, *J*=5.5 Hz, H_3), 3.78-3.86 (m, 1H), 3.38-3.51 (m, 2H), 1.90-2.07 (m, 1H), 1.42-1.70 (m, 3H). Anal.Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.25; H, 7.58.

Reaction of Epoxides 5-8 with $LiAlH_4$ in the Presence of 12-Crown-4. General procedure. A suspension of $LiAlH_4$ (0.039 g, 1.0 mmol) in pentane (3.0 ml) was treated with 12-crown-4 (0.18 ml, 1.1 mmol) and the mixture was stirred at r.t. for 15 h. The epoxide (0.50 mmol) in pentane (1.0 ml) was added and the reaction mixture was stirred for 5 h at r.t. Usual workup afforded a crude reaction product which was analyzed by GC and ^1H NMR to give the results shown in Tables 1 and 2.

References and Notes

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13. Given that there are three oxygens in epoxides **7** and **8** (X=O), other chelate structures than **64** and **68** from **7** (Scheme 3) and **70** from **8** (Scheme 4) are obviously possible (and probable) in solution under metal salt-promoted reaction conditions. However, chelates other than **64**, **68**, and **70** should not reasonably affect the regiochemical outcome of the ring opening of epoxides **7** and **8**, respectively, and are consequently not considered in the mechanistic discussion.

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