Regiochemical Control of the Ring Opening of 1,2-Epoxides by Means of Chelating Processes. 5.[1] Synthesis and Reactions of Some 2,3-Epoxy-1-alkanol Derivatives

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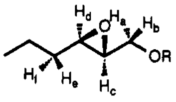
In order to study the effect of a remote polar functionality on the regiochemistry of the ring opening of aliphatic epoxides, the synthesis and some nucleophilic additions (methanolysis, azidolysis, and aminolysis) of suitable 2,3-epoxy-1-alkanol derivatives (epoxides *trans*-**1a–d** and *cis*-**2**) were carried out. The C-3 selectivity commonly observed when nonchelating ring opening conditions are used is lower than when the epoxides are allowed to react in the presence of metal ions (Li^+, Mg^{2+}, Zn^{2+}) due to the probable intervention of bidentate-chelated intermediates in the latter case, and in some instances an almost complete C-3 regioselection is obtained. Under identical conditions involving chelation control, trans epoxide **1a** shows higher C-3 selectivity than cis isomer **2**. A free hydroxyl functionality is not necessary in order to observe chelation-controlled regioselectivity in the epoxides that we examined.

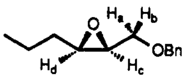
The stereo- and regiocontrolled addition of suitable nucleophiles to 1,2-epoxides can in theory be helpful for the stereoselective synthesis of complex polyfunctional molecules. Whereas the stereoselectivity of the ring opening of 1,2-epoxides is usually completely anti,[2,3] regioselectivity control is not always simple, especially in the case of 1,2-disubstituted examples.

In previously described works, the introduction of a polar heterofunctionality (OR) in the β-position of a conformationally semirigid cycloaliphatic oxirane system turned out to be efficacious in directing the regiochemistry of the addition process by allowing the elective use of either metal-assisted chelating or nonchelating reaction conditions.[4] Regiochemical control was achieved in epoxide ring-opening reactions with several nucleophiles (CH_3^-,[4a] H^-,[4b] CH_3OH,[4b] Cl^-,[4b] amines,[4c] N_3^-,[4c] $PhC{\equiv}C^-$[4d]). However, when the ring opening of aliphatic β-alkoxy oxiranes was examined, we found that the regioselectivity was significantly affected by chelating procedures only in the case of organometallic additions in nonpolar solvents,[5] other reaction conditions such as $CH_3OH/CH_3O^-M^+$ being essentially unselective.[6]

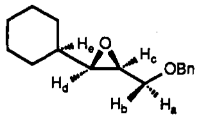
Important results obtained by Sharpless et al. on 2,3-epoxy-1-alkanol derivatives were indicative of chelative regioselection control in these systems by means of Ti(IV).[7,8] The data were taken from several reactions (with the exception of methanolysis), but the method appeared to be fully operative only when a free alcoholic function was present.[7,8] Consequently, we have studied the ring-opening reactions (methanolysis, azidolysis, and aminolysis) of epoxy benzyl ethers **1a**,[8] **1c**, **1d**, and **2** as well as epoxy alcohol **1b**.[8,9]



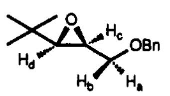
1a, R = Bn
1b, R = H



2



1c



1d

Results

Epoxides **1a** and **2** were prepared by *m*-chloroperoxybenzoic acid (*m*-CPBA) oxidation of the benzyl ethers **4** and **6** obtained by benzylation of the commercially available alcohols **3** and **5**, respectively. The direct epoxidation of **3** with *m*-CPBA yielded the epoxide **1b**.[8] The synthesis of the epoxides **1c** and **1d** was accomplished by oxidation of benzyl ethers **11c** and **11d** with *m*-CPBA. In this case, the necessary unsaturated trans alcohols **10c** and **10d** were obtained by DIBAL reduction of the corresponding esters **9c**[10a] and **9d**.[10b] Esters **9c** and **9d** were selectively synthesized by reaction of the aldehydes **7c** and **7d**, respectively, with the stabilized Wittig reagent obtained from **8** in a nonpolar solvent[11] (Scheme I).[9]

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(1) Preceding paper in this series: Chini, M.; Crotti, P.; Flippin, L. A.; Gardelli, C.; Macchia, F. *J. Org. Chem.* **1992**, *57*, 1713.

(2) Buchanan, J. G.; Sable, H. Z. In *Selective Organic Transformation*; Thyagarajan, B. S., Ed.; Wiley Interscience: New York, 1972; Vol. 1, p 1.

(3) Barili, P. L.; Bellucci, G.; Macchia, B.; Macchia, F.; Parmigiani, G. *Gazz. Chim. Ital.* **1971**, *101*, 300.

(4) (a) Chini, M.; Crotti, P.; Flippin, L. A.; Macchia, F. *Tetrahedron Lett.* **1989**, *30*, 6563; (b) *J. Org. Chem.* **1990**, *55*, 4265. (c) *Ibid.* **1991**, *56*, 7043. (d) Chini, M.; Crotti, P.; Favero, L.; Macchia, F. *Tetrahedron Lett.* **1991**, *32*, 6617.

(5) Flippin, L. A.; Brown, P. A.; Jalali-Araghi, K. *J. Org. Chem.* **1989**, *54*, 3588.

(6) Unpublished results from these laboratories.

(7) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1560. See also: Martin, V. S.; Ode, J. M.; Palazon, J. M.; Soler, M. A. *Tetrahedron: Asymmetry* **1992**, *3*, 573.

(8) Caron, M.; Carlier, P. R.; Sharpless, K. B. *J. Org. Chem.* **1988**, *53*, 5185.

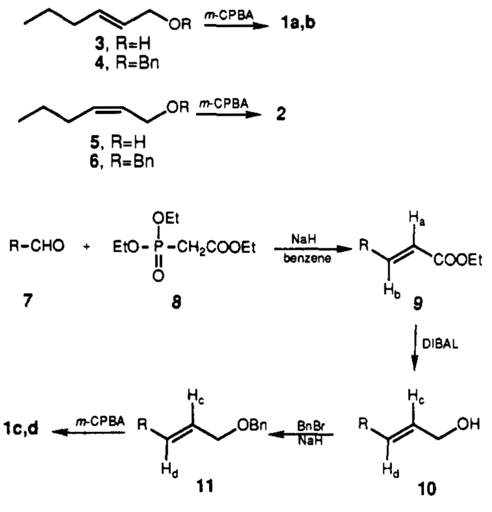
(9) All the structures depicted in the formulas and in Schemes I–III represent one enantiomeric series of the racemic mixtures used in this study.

(10) (a) Matsui, S. *Bull. Chem. Soc. Jpn* **1984**, *57*, 426. (b) Andruszkiewicz, R.; Silverman, R. B. *Synthesis* **1989**, 953.

(11) (a) Cadogan, J. I. G. *Organophosphorus Reagents in Organic Synthesis*; Academic Press: New York, 1979. (b) Bestmann, H. J. *Pure Appl. Chem.* **1979**, *51*, 515.

0022-3263/93/1958-1221$04.00/0

Scheme I



c, R = c-C_6H_{11}; d, R = t-butyl

The results of ring opening of epoxides **1a–d** and **2** under a variety of reaction conditions are summarized in Tables I and II. The determination of relative amounts of the regioisomeric *C-2-* (**12a–d** and **16**) and *C-3-type products*[12] (**13a–d** and **17**) was accomplished by combined GC and ^{1}H NMR analysis of the acetylated crude reaction products that contained corresponding mixtures of **14a–d** and **15a–d**, from trans epoxides **1a–d**, and **18** and **19**, from cis epoxide **2** (Scheme II).[9] The acetylation step was necessary in order both to improve the separation of the pairs of regioisomers in GC analysis and to clarify the signals of protons H_c and/or H_d in the ^{1}H NMR spectra of the products. These proton signals have been unequivocally assigned by double resonance experiments, irradiating the quite distinct signal of the proton α to the acetyl group.[13]

As expected on the basis of Sharpless' results obtained with epoxy alcohol **1b**,[8] a prevalence of nucleophilic attack on C-3 was observed in the reactions of trans epoxy ether **1a** carried out under nonchelating conditions (H^+/MeOH and MeONa/MeOH for methanolysis, NaN_3/NH_4Cl for azidolysis, and $NHEt_2$/EtOH for aminolysis, Table I). However, when epoxide **1a** was allowed to react in the presence of metal ions (Li^+, Mg^{2+}, Zn^{2+}), an increase of C-3 nucleophilic attack was observed in all the reactions studied. This increase appeared to be largely dependent on the type and amount of the metal ion (Table I). In some cases (entries 9 and 11, Table I) a complete or practically complete C-3 regioselection was obtained. Analogous behavior was observed for the reactions of cis epoxide **2** (see Table II), although the effectiveness of the metal ion in favoring C-3 selectivity was lower than in the case of the corresponding trans epoxide **1a**. Our results from trans epoxy alcohol **1b** ring openings (Table I) further confirm a metal ion-dependent selectivity for C-3 attack.

The reactions of the cyclohexyl-substituted epoxide **1c** under nonchelating conditions were less C-3 selective than **1a**, probably as a consequence of the larger steric hindrance present on the C-3 oxirane carbon of **1c**; however, an increase in the C-3 selectivity was found when metal ion catalytic ring opening conditions were used (Table I).

In the case of *tert*-butyl-substituted epoxide **1d**, the very high steric crowding at C-3 emphatically disfavored nucleophilic attack on that carbon under all conditions tried (entries 28–34, Table I); however, the metal ion-catalyzed methanolysis and azidolysis of epoxide **1d** showed a significant increase in the amount of C-3 attack (entries 30 and 32, Table I). Interestingly, the $LiClO_4$-catalyzed aminolysis of **1d** occurred in good yield (entry 34, Table I), although the regiochemistry of attack was exclusively on the C-2 carbon; this result is in contrast to an uncatalyzed aminolysis attempt that failed completely (entry 33, Table I).

Discussion

The above results indicate that metal salts affect the regiochemistry of some ring-opening reactions (azidolysis, methanolysis, and aminolysis) of 1-alkoxy-2,3-epoxyalkanes (epoxides **1a–d** and **2**). An increase in C-3 nucleophilic attack is generally observed in the metal salt-catalyzed reactions that, in the case of epoxide **1a**, can lead to practically complete C-3 regioselection (entries 9 and 11, Table I). This effect is probably due to the intervention of bidentate-chelated structures of type **20**[14] (from trans epoxides **1a–d**) and **21** (from cis epoxide **2**) (Scheme III) in which the metal cation is coordinated both to the oxirane and to the alkoxide oxygen. These bidentate structures (**20** and **21**) are similar to the ones suggested for the methylating ring opening of 1-alkoxy-2,3-epoxyalkanes[15] and for the Ti(IV)-mediated azidolysis of 2,3-epoxy-1-alkanols.[7,8] The increase in C-3 selectivity (route *a*, Scheme III) in the ring opening of epoxides **1a–d** and **2** through intermediates **20** and **21**, respectively, may be rationalized by invoking stereoelectronic factors similar to those implicated in the chelation-controlled ring opening of 3,4-epoxy-1-alkanol derivatives.[5] The lower efficiency of metal ions in promoting the C-3 selectivity of the cis epoxide **2** compared with that observed in the reactions of the corresponding trans isomer **1a** can be rationalized on the basis of the incursion of two new eclipsing interactions (between **M** and a methylene group) in the formation of the chelate intermediate **21** from the cis epoxide **2**;[5] only one of these repulsive interactions is necessarily present in the formation of the similar intermediate **20** from the trans epoxide **1a**. Moreover, the formation of the conformationally restricted chelate structure **21** from the cis isomer **2** may cause an increase in strain between the C-1 and C-4 methylene groups (Scheme III).

A comparison of the reaction of trans epoxides **1a**, **1c**, and **1d** indicates that an increase in the steric hindrance at C-3 results in a general decrease in C-3 selectivity, as expected.[8] However, when metal salt-catalyzed reaction conditions are used in methanolysis and azidolysis, an increase in C-3 selectivity occurs. The only exception is the metal salt-catalyzed aminolysis of **1d** with $NHEt_2$, in which only the C-2-type product is observed (entry 34, Table I). Evidently in this case, where the nonchelating aminolysis conditions ($NHEt_2$/EtOH, refluxing) failed even after several days' heating, the strong catalytic effect

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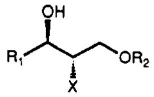
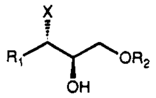
[12] The C-2- and C-3-type product nomenclature refers to the attacking site of the nucleophile (i.e., at the C-2 or C-3 oxirane carbon of both **1a–d** and **2**) in accordance with the numbering scheme shown in Schemes II and III.

[13] Jackman, L. M.; Sternhell, S. *Application of Nuclear Magnetic Resonance Spectroscopy to Organic Chemistry*, 2nd ed.; Pergamon Press: London, 1969; p 151.

[14] For the sake of simplicity, only the generic structure **20** is shown in Scheme III, valid for all trans epoxides **1a–d**.

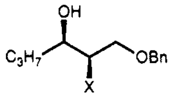
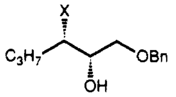
[15] Pfaltz, A.; Mattenberger, A. *Angew. Chem. Suppl.* **1982**, 161.

Table I. Regioselectivity (%) of the Ring-Opening Reactions of Trans Epoxides 1a–d

entry	epoxide	reagents	react. condns[a] (°C)	react. time (h)	C-2-type product[b] 	C-3-type product[b] 
1	**1a**	MeOH/H^+	A (rt)	1	19[c]	81[d]
2	**1a**	MeONa	B (60)	18	20[c]	80[d]
3	**1a**	MeOH/$LiClO_4$	C (60)	24	11[c]	89[d]
4	**1a**	MeOH/$Mg(ClO_4)_2$	C (80)	24	8[c]	92[d]
5	**1a**	NaN_3/NH_4Cl	D (80)	18	13[e]	87[f]
6	**1a**	$NaN_3/LiClO_4$	E (80)	18	6[e]	94[f]
7	**1a**		F (80)	18	5[e]	95[f]
8	**1a**		G (80)	18	4[e]	96[f]
9	**1a**		H (80)	18	3[e]	97[f]
10	**1a**	$NaN_3/Mg(ClO_4)_2$	E (80)	18	6[e]	94[f]
11	**1a**	$NaN_3/Zn(OSO_2CF_3)_2$	E (80)	18	2[e]	98[f]
12	**1a**	$NaN_3/NaClO_4$	E (80)	10 days	no reaction	
13	**1a**	$NHEt_2$	I (80)	18	13[g]	87[h]
14	**1a**	$NHEt_2/LiClO_4$	J (rt)	24	<1[g]	>99[h]
15	**1b**	MeOH/H^+	A (rt)	1	24[i]	76[j]
16	**1b**	MeOH/$LiClO_4$	C (80)	36	8[i]	92[j]
17	**1b**	NaN_3/NH_4Cl	D (80)	24	15[k]	85[l]
18	**1b**	$NaN_3/LiClO_4$	F (80)	18	6[k]	94[l]
19	**1b**	$NHEt_2$	I (80)	18	27[m]	73[n]
20	**1b**	$NHEt_2/LiClO_4$	J (80)	18	11[m]	89[n]
21	**1c**	MeOH/H^+	A (rt)	1	32[o]	68[p]
22	**1c**	MeONa	B (80)	96	39[o]	61[p]
23	**1c**	MeOH/$LiClO_4$	C (80)	96	15[o]	85[p]
24	**1c**	NaN_3/NH_4Cl	D (80)	6 days	17[q]	83[r]
25	**1c**	$NaN_3/LiClO_4$	F (80)	96	5[q]	95[r]
26	**1c**	$NHEt_2$	I (80)	7 days	17[s]	83[t]
27	**1c**	$NHEt_2/LiClO_4$	J (80)	7 days	9[s]	91[t]
28	**1d**	MeOH/H^+	A (rt)	1	93[u]	7[v]
29	**1d**	MeONa	B (80)	6 days	98[u]	2[v]
30	**1d**	MeOH/$LiClO_4$	C (80)	6 days	82[u]	18[v]
31	**1d**	NaN_3/NH_4Cl	D (80)	5 days	93[w]	7[x]
32	**1d**	$NaN_3/LiClO_4$	K (120)	80	60[w]	40[x]
33	**1d**	$NHEt_2$	I (80)	7 days	no reaction	
34	**1d**	$NHEt_2/LiClO_4$	J (80)	7 days	>99[y]	<1

[a] Conditions: A, 0.2 N H_2SO_4; B, epoxide:MeONa = 1:60; C, 10 M ($LiClO_4$) or 1 M [$Mg(ClO_4)_2$] metal salt in anhydrous MeOH; D, MeOH/H_2O (8:1), see ref 7; E, MeCN, 1 M metal salt, see ref 4c; F, as in E with 2 M $LiClO_4$; G, as in E, with 5 M $LiClO_4$; H, as in E with 10 M $LiClO_4$; I, EtOH, epoxide:amine = 1:10; J, MeCN, epoxide:amine:$LiClO_4$ = 1:10:10, see ref 4c; K, diglyme, 2 M $LiClO_4$, see ref 4c. [b] See ref 12. R_1 = $CH_3(CH_2)_2$ from **1a** and **1b**; R_1 = *c*-C_6H_{11} from **1c**; R_1 = *tert*-butyl from **1d**; R_2 = Bn from **1a**, **1c**, and **1d**; R_2 = H from **1b**. The regiochemical composition was determined by GC and ^1H NMR analysis of the corresponding crude acetylated ring-opening reaction product. [c] Methoxy alcohol **12a**, X = OMe. [d] Methoxy alcohol **13a**, X = OMe. [e] Azido alcohol **12a**, X = N_3. [f] Azido alcohol **13a**, X = N_3. [g] Amino alcohol **12a**, X = NEt_2. [h] Amino alcohol **13a**, X = NEt_2. [i] Methoxy diol **12b**, X = OMe. [j] Methoxy diol **13b**, X = OMe. [k] Azido diol **12b**, X = N_3. [l] Azido diol **13b**, X = N_3. [m] Amino diol **12b**, X = NEt_2. [n] Amino diol **13b**, X = NEt_2. [o] Methoxy alcohol **12c**, X = OMe. [p] Methoxy alcohol **13c**, X = OMe. [q] Azido alcohol **12c**, X = N_3. [r] Azido alcohol **13c**, X = N_3. [s] Amino alcohol **12c**, X = NEt_2. [t] Amino alcohol **13c**, X = NEt_2. [u] Methoxy alcohol **12d**, X = OMe. [v] Methoxy alcohol **13d**, X = OMe. [w] Azido alcohol **12d**, X = N_3. [x] Azido alcohol **13d**, X = N_3. [y] Amino alcohol **12d**, X = NEt_2.

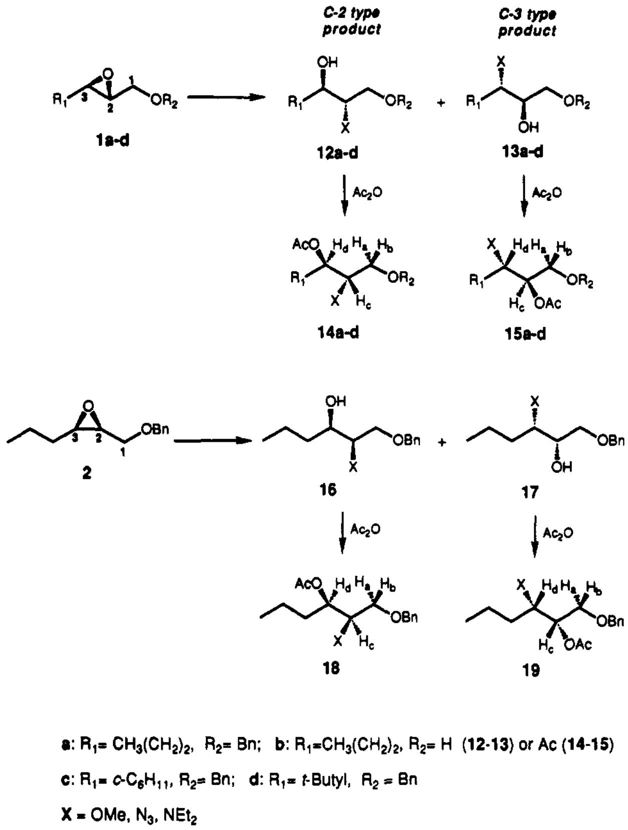
Table II. Regioselectivity (%) of the Ring-Opening Reactions of Cis Epoxide 2

entry	reagents	react. condns[a]	react. time (h)	C-2-type product[b] 	C-3-type product[b] 
1	MeOH/H^+	A (rt)	1	19[c]	81[d]
2	MeONa	B (60)	18	29[c]	71[d]
3	MeOH/$LiClO_4$	C (60)	48	17[c]	83[d]
4	NaN_3/NH_4Cl	D (80)	18	17[e]	83[f]
5	$NaN_3/LiClO_4$	E (80)	48	8[e]	92[f]
6		F (80)	18	8[e]	92[f]
7	$NaN_3/Mg(ClO_4)_2$	E (80)	48	4[e]	96[f]
8	$NaN_3/Zn(OSO_2CF_3)_2$	E (80)	36	14[e]	86[f]
9	$NaN_3/NaClO_4$	E (80)	7 days	no reaction	
10	$NHEt_2$	I (80)	18	18[g]	82[h]
11	$NHEt_2/LiClO_4$	J (rt)	24	12[g]	88[h]

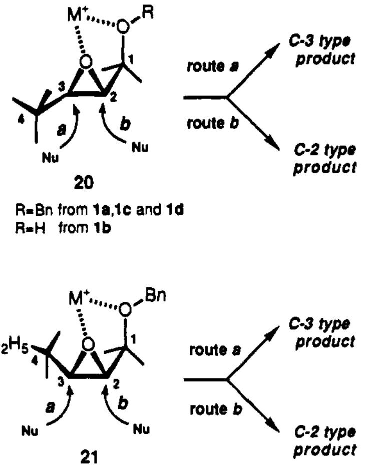
[a] Conditions, see footnote *a*, Table I. [b] See ref 12. [c] Methoxy alcohol **16**, X = OMe. [d] Methoxy alcohol **17**, X = OMe. [e] Azido alcohol **16**, X = N_3. [f] Azido alcohol **17**, X = N_3. [g] Amino alcohol **16**, X = NEt_2. [h] Amino alcohol **17**, X = NEt_2.

of the metal salt[16] is successful in giving the aminolysis product, but the larger steric requirement of the nucleophile ($NHEt_2$) prevents any substitution pathway on the neopentyl C-3 carbon.

Scheme II



Scheme III



A comparison of the reactions of the trans epoxy ether **1a** with those of epoxy alcohol **1b** (Table I) shows a very similar regioselectivity behavior of the two epoxides on passing from nonchelating to metal salt-catalyzed reaction conditions. Evidently in these systems and with our methodology it is not necessary to have a free hydroxyl function in order to observe chelation-controlled C-3 selectivity in oxirane ring openings. On the contrary, in the Ti(IV)-mediated azidolysis and aminolysis of epoxides **1a** and **1b**,[7,8] a free hydroxyl functionality has been reported to be essential: in these conditions, epoxy ether **1a** gave either no reaction or, under forcing conditions, quite low yields.[7,8,17]

In principle, selectivity for C-3 nucleophilic attack in the chelation-controlled reactions of epoxides **1a–d** and **2** should correlate with the Lewis acidity and ionic radius of the metal cations employed. In fact, compounds **1a–c** and **2** exhibit a pronounced intrinsic preference for C-3 attack even under nonchelating reaction conditions (CH_3OH/H^+, CH_3ONa/CH_3OH, $NaN_3/NH_4Cl/CH_3OH-H_2O$, and $Et_2NH/EtOH$); thus, the range of metal cation effects on reactions of **1a–c** and **2** was generally small, but significant.

In conclusion, all of the epoxides that we studied showed a definite tendency toward higher C-3 selectivity when a Lewis-acidic metal cation (Li^+, Mg^{2+}, or Zn^{2+}) was added to the reaction mixture. Even the high intrinsic preference for C-2 attack exhibited by epoxide **1d** was moderated (although not actually reversed) in two such examples (entries 30 and 32, Table I).

Experimental Section

For general experimental information, see ref 4b. General procedure for acetylation: the crude reaction product (0.10 g) in anhydrous pyridine (2 mL) was treated at 0 °C with Ac_2O (1 mL) and then left for 24 h at rt. Ice was added, and after 5 h, dilution with water, extraction with ether, and evaporation of the washed [water, 10% aqueous HCl (excepted for the aminolysis reactions), saturated aqueous $NaHCO_3$, and water] ether extracts afforded a crude reaction product containing the acetylated regioisomeric opening products. In all cases the crude acetylated product was subjected to preparative TLC in order to separate pure the two regioisomers [a 7:3 hexane/Et_2O (methoxy and azido derivatives), or a 7:3 hexane/diisopropyl ether (diethylamino derivatives) mixture was used as the eluant]. From the same reaction mixtures it was not possible to separate pure compounds **14a** ($X = N_3$), **14b** ($X = N_3$, $R_2 = Ac$), **14c** ($X = N_3$), **14c** ($X = NEt_2$), and **18** ($X = OMe$ and $X = N_3$); however, their presence in the crude reaction products was substantiated by GC and ^1H NMR analysis.

Ethyl *trans*-3-Cyclohexyl-2-propenoate (9c). A solution of triethyl phosphonoacetate (22.5 g, 0.11 mol) in anhydrous toluene (80 mL) was added dropwise with stirring over 1 h at rt to a suspension of NaH (2.64 g of an 80% dispersion in mineral oil, 0.11 mol) in anhydrous toluene (30 mL). The reaction mixture was cooled at −20 °C then treated dropwise with a solution of cyclohexanecarboxaldehyde (**7c**) (12.3 g, 0.11 mol) in anhydrous toluene (20 mL): during the addition the reaction temperature was kept below −10 °C. The reaction mixture was stirred for 30 min at the same temperature and then diluted with ether. Evaporation of the washed (water, saturated aqueous $NaHCO_3$, and water) organic solution afforded a crude oil (18.0 g) essentially consisting of ester **9c**[10a] (82% yield) which was directly used in the next step.

Ethyl *trans*-4,4-Dimethyl-2-pentenoate (9d). Following the procedure previously described above for the preparation of **9c**, the reaction of pivalaldehyde (**7d**) (8.61 g, 0.10 mol) with the ylide derived from triethyl phosphonoacetate (22.5 g, 0.11 mol) and NaH (2.64 g of a 80% dispersion in mineral oil, 0.11 mol) afforded ester **9d**[10b] (14.9 g, 96% yield) practically pure, which was directly used in the next step without any further purification.

Synthesis of Alcohols 10c and 10d. General Procedure. In an inert atmosphere, 1 M DIBAL in hexane (71 mL) was added dropwise under stirring to a cooled (−20 °C) solution of the ester (**9c** or **9d**) (35.0 mmol) in anhydrous Et_2O (230 mL). When the addition was complete, the reaction mixture was allowed to warm to rt, and then MeOH (5 mL) was added. Evaporation of the washed (water, 5% aqueous HCl, and water) organic solution

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(16) (a) Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.* **1990**, *31*, 4661; (b) *J. Org. Chem.* **1991**, *56*, 5939.

(17) Control experiments carried out by us on epoxy ethers **1c**, **1d**, and **2** with $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ in anhydrous benzene at 70 °C for 20 h in accordance with ref 8 yielded complex mixtures containing the addition products with the following C-2/C-3 selectivity: **1c**, 8:92 (55% yield); **2**, <1:>99 (30% yield); **1d**, no reaction.[18]

(18) It is puzzling that Ti(IV), an extremely oxophilic species, does not give satisfactory yields in the chelation-controlled ring-opening of epoxy ethers as metal cations, such as Li^+, Mg^{2+}, and Zn^{2+} do. Possibly, the large difference in mole ratio of metal cation used in the present study (5–10:1) is the significant difference.

afforded an oily residue consisting of the corresponding alcohol (GC and ^{1}H NMR) which was distilled.

***trans*-3-Cyclohexyl-2-propen-1-ol (10c)**: a liquid (4.9 g, 85% yield); bp 65 °C (0.5 mmHg); IR 3300 cm^{-1} (OH); ^{1}H NMR δ 5.63 (dd, 1 H, J_{cd} = 15.6 and J_{de} = 5.3 Hz, H_d), 5.55 (ddd, 1 H, J_{cd} = 15.6, J_{ac} = 4.6 and J_{ab} = 4.3 Hz, H_c), 4.07 and 4.05 (ABdd, 2 H, J = 4.6 Hz), 2.57 (m, 1 H), 1.59–1.78 (m, 4 H), 0.96–1.26 (m, 6 H). Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.15; H, 11.37.

***trans*-4,4-Dimethyl-2-penten-1-ol (10d)**: a liquid (3.85 g, 75% yield); bp 31–32 °C (0.2 mmHg); IR 3280 cm^{-1} (OH); ^{1}H NMR δ 5.64 (dd, 1 H, J_{cd} = 15.7, J_{ad} = J_{bd} = 1.2 Hz, H_d), 5.46 (ddd, 1 H, J_{cd} = 15.7, J_{bc} = J_{ac} = 5.7 Hz, H_c), 4.03 and 4.02 (ABdd, 2 H, J = 5.7 Hz), 0.95 (s, 9 H). Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.60; H, 12.54.

Benzylation of Alcohols 3, 5, 10c, and 10d. General Procedure. A suspension of NaH (7.0 g of a 80% dispersion in mineral oil, 0.23 mol) in anhydrous THF (150 mL) was treated at 50 °C with a solution of benzyl bromide (14.5 mL, 0.12 mol) in anhydrous THF (20 mL). A solution of the alcohol (0.10 mol) in anhydrous THF (150 mL) was then added dropwise over 1 h, and the reaction mixture was maintained at 50–60 °C for 18 h. After the mixture was cooled, water was carefully added in order to destroy the excess of hydride. Dilution with ether and evaporation of the washed (water) organic solution afforded a crude benzyl ether which was distilled to give the pure ether (GC and ^{1}H NMR).

***trans*-1-(Benzyloxy)-2-hexene (4)**: 18.76 g, 98% yield; bp 71 °C (0.2 mmHg); ^{1}H NMR δ 7.23–7.37 (m, 5 H), 5.53–5.56 (m, 2 H), 4.58 (m, 2 H), 4.06 (m, 2 H), 1.97–2.07 (m, 2 H), 1.31–1.49 (m, 2 H), 0.90 (t, 3 H, J = 7.3 Hz). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.25; H, 9.84.

***cis*-1-(Benzyloxy)-2-hexene (6)**: 18.32 g, 96% yield; bp 73 °C (0.2 mmHg); ^{1}H NMR δ 7.23–7.37 (m, 5 H), 5.45–5.66 (m, 2 H), 4.58 (m, 2 H), 4.16–4.19 (m, 2 H), 1.99–2.46 (m, 2 H), 1.30–1.48 (m, 2 H), 0.90 (t, 3 H, J = 7.3 Hz). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.31; H, 8.46.

***trans*-1-(Benzyloxy)-3-cyclohexyl-2-propene (11c)**: 28.0 g, 90% yield; bp 118 °C (0.15 mmHg); ^{1}H NMR δ 7.21–7.35 (m, 5 H), 6.65 (dd, 1 H, J_{cd} = 15.55, J_{de} = 5.82 Hz, H_d), 5.52 (ddd, 1 H, J_{cd} = 15.6 and J_{ac} = J_{cb} = 5.8 Hz, H_c), 4.49 (s, 2 H), 3.96 (d, 2 H, J = 5.7 Hz), 1.56–1.78 (m, 5 H), 0.96–1.25 (m, 6 H). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.54; H, 9.36.

***trans*-1-(Benzyloxy)-4,4-dimethyl-2-pentene (11d)**: 19.78 g, 97% yield; bp 75 °C (0.4 mmHg); ^{1}H NMR δ 7.29–7.42 (m, 5 H), 5.77 (ddd, 1 H, J_{cd} = 15.6, J_{ad} = J_{bd} = 1.0 Hz, H_d), 5.53 (ddd, 1 H, J_{cd} = 15.6 and J_{ac} = J_{bc} = 6.1 Hz, H_c), 4.58 (s, 2 H), 3.98 (m, 2 H), 1.06 (s, 9 H). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.45; H, 9.74.

Synthesis of Epoxides 1a–d and 2. General Procedure. A solution of the olefin (**4**, **6**, **11c**, or **11d**) (50.0 mmol) in anhydrous CH_2Cl_2 (400 mL) was treated with 50% *m*-CPBA (19.85 g, 57.5 mmol) at 0 °C under stirring for 16 h. 5% Aqueous $Na_2S_2O_3$ (100 mL) was added at the same temperature, and the reaction mixture was stirred for 20 min. Evaporation of the washed (5% aqueous NaOH, and water) organic solution afforded a liquid residue consisting of the corresponding pure epoxide.

***trans*-2,3-Epoxy-1-(benzyloxy)hexane (1a)**: a liquid (9.4 g, 91% yield); ^{1}H NMR δ 7.25–7.37 (m, 5 H), 4.61 and 4.53 (ABdd, 2 H, J = 11.9 Hz), 3.72 (dd, 1 H, J_{ac} = 3.3, J_{ab} = 11.4 Hz, H_a), 3.46 (dd, 1 H, J_{bc} = 5.6, and J_{ab} = 11.4 Hz, H_b), 2.95 (ddd, 1 H, J_{ac} = 3.3, J_{bc} = 5.6 and J_{cd} = 2.3 Hz, H_c), 2.83 (ddd, 1 H, J_{cd} = 2.3 and J_{de} = J_{df} = 5.3 Hz, H_d). Anal. Calcd for $C_{13}H_{18}O_2$: C, 82.06; H, 8.79. Found: C, 82.14; H, 8.55.

***trans*-2,3-Epoxy-1-hexanol (1b)**: a low-melting product (5.2 g, 89% yield); IR 3420 cm^{-1} (OH); ^{1}H NMR δ 3.91 (dd, 1 H, J_{ac} = 3.4 and J_{ab} = 12.6 Hz, H_a), 3.60 (dd, 1 H, J_{bc} = 4.5, and J_{ab} = 12.6 Hz, H_b), 2.90–2.99 (m, 2 H, H_c and H_d), 1.40–1.58 (m, 4 H), 0.96 (dd, 3 H, J = 7.1 and 6.1 Hz). Anal. Calcd for $C_6H_{12}O_2$: C, 62.04; H, 10.41. Found: C, 62.35; H, 10.54.

***trans*-1-(Benzyloxy)-3-cyclohexyl-2,3-epoxypropane (1c)**: a liquid (13.7 g, 96% yield); ^{1}H NMR δ 7.20–7.29 (m, 5 H), 4.52 and 4.47 (ABdd, 2 H, J = 15.3 Hz), 3.63 (dd, 1 H, J_{ac} = 3.2 and J_{ab} = 11.4 Hz, H_a), 3.35 (dd, 1 H, J_{bc} = 5.8, J_{ab} = 11.4 Hz, H_b), 2.92 (ddd, 1 H, J_{ac} = 3.2, J_{bc} = 5.8, J_{cd} = 2.3 Hz, H_c), 2.54 (dd, 1 H, J_{cd} = 2.3 and J_{de} = 6.4 Hz, H_d), 1.59–1.78 (m, 5 H), 0.96–1.25 (m, 6 H). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.31; H, 9.39.

***trans*-1-(Benzyloxy)-4,4-dimethyl-2,3-epoxypentane (1d)**: a liquid (10.64 g, 96% yield); ^{1}H NMR δ 7.26–7.37 (m, 5 H), 4.62 and 4.54 (ABdd, 2 H, J = 11.9 Hz), 3.74 (dd, 1 H, J_{ac} = 3.1 and J_{ab} = 11.4 Hz, H_a), 3.43 (dd, 1 H, J_{bc} = 6.0 and J_{ab} = 11.4 Hz, H_b), 3.07 (ddd, 1 H, J_{ac} = 3.1, J_{bc} = 6.0, and J_{cd} = 2.4 Hz, H_c), 2.63 (d, 1 H, J_{cd} = 2.4 Hz, H_d), 0.93 (s, 9 H). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.42; H, 9.43.

***cis*-2,3-Epoxy-1-(benzyloxy)hexane (2)**: a liquid (9.25 g, 90% yield); ^{1}H NMR δ 7.25–7.37 (m, 5 H), 4.65 and 4.52 (ABdd, 2 H, J = 11.8 Hz), 3.70 (dd, 1 H, J_{ac} = 4.4 and J_{ab} = 11.0 Hz, H_a), 3.53 (dd, 1 H, J_{bc} = 6.3 and J_{ab} = 11.0 Hz, H_b), 3.19 (ddd, 1 H, J_{ac} = J_{cd} = 4.4 and J_{bc} = 6.3 Hz, H_c), 2.98 (m, 1 H, H_d). Anal. Calcd for $C_{13}H_{18}O_2$: C, 82.06; H, 8.79. Found: C, 82.30; H, 8.75.

H^+-Catalyzed Methanolysis of Epoxides 1a–d and 2. General Procedure. The epoxide (1.0 mmol) was added to a 0.2 N H_2SO_4 in anhydrous MeOH (5 mL), and the reaction mixture was stirred for 1 h at rt. Dilution with water, extraction with ether, and evaporation of the washed (saturated aqueous $NaHCO_3$, and water) ether extracts afforded a crude reaction mixture which was acetylated and then analyzed by GC and ^{1}H NMR.

The crude acetylated product (0.25 g) from **1a** gave pure **14a** (0.020 g) and **15a (X = OMe)** (0.11 g).

***anti*-2-Acetoxy-1-(benzyloxy)-3-methoxyhexane (15a, X = OMe)**: a liquid; IR 1740 cm^{-1} (C═O); ^{1}H NMR δ 7.23–7.37 (m, 5 H), 5.16 (ddd, 1 H, J_{ac} = J_{cd} = 4.4 and J_{bc} = 5.8 Hz, H_c), 4.56 and 4.49 (ABdd, 2 H, J = 12.2 Hz), 3.66 (dd, 1 H, J_{ac} = 4.4 and J_{ab} = 10.7 Hz, H_a), 3.59 (dd, 1 H, J_{bc} = 5.8 and J_{ab} = 10.7 Hz, H_b) 3.33–3.46 (m, 1 H, H_d), 3.37 (s, 3 H), 2.08 (s, 3 H), 1.29–1.54 (m, 4 H), 0.91 (t, 3 H, J = 6.9 Hz). Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.62. Found: C, 68.26; H, 8.91.

***anti*-3-Acetoxy-1-(benzyloxy)-2-methoxyhexane (14a, X = OMe)**: a liquid; IR 1740 cm^{-1} (C═O); ^{1}H NMR δ 7.25–7.35 (m, 5 H), 5.13 (m, 1 H), 4.51 and 4.59 (ABdd, 2 H, J = 15.9 Hz), 3.55 (m, 2 H), 3.46 (s, 3 H), 3.47 (m, 1 H), 2.03 (s, 3 H), 1.21–1.69 (m, 4 H), 0.90 (t, 3 H, J = 7.1 Hz). Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.62. Found: C, 68.29; H, 8.47.

The crude acetylated product (0.22 g) from **1b** gave pure **14b** (0.030 g) and **15b (X = OMe)** (0.13 g).

***anti*-1,2-Diacetoxy-3-methoxyhexane (15b, X = OMe, R_2 = Ac)**: a liquid; IR 1740 cm^{-1} (C═O); ^{1}H NMR δ 5.14 (ddd, 1 H, J_{ac} = 3.0, J_{bc} = 7.4 and J_{cd} = 4.3 Hz, H_c), 4.37 (dd, 1 H, J_{ac} = 3.0 and J_{ab} = 12.1 Hz, H_a), 4.14 (dd, 1 H, J_{bc} = 7.4 and J_{ab} = 12.1 Hz, H_b), 3.40 (s, 3 H), 3.29–3.37 (m, 1 H), 2.10 (s, 3 H), 2.05 (s, 3 H), 1.25–1.71 (m, 4 H), 0.93 (t, 3 H, J = 7.0 Hz). Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 56.95; H, 8.71.

***anti*-1,3-Diacetoxy-2-methoxyhexane (14b, X = OMe, R_2 = Ac)**: a liquid; IR 1742 cm^{-1} (C═O); ^{1}H NMR δ 5.09 (m, 1 H), 4.24 (dd, 1 H, J_{ac} = 3.7 and J_{ab} = 12.0 Hz, H_a), 4.10 (dd, 1 H, J_{bc} = 6.2 and J_{ab} = 12.0 Hz, H_b), 3.45 (s, 3 H), 3.40 (m, 1 H), 2.09 (s, 3 H), 2.06 (s, 3 H), 1.28–1.68 (m, 4 H). Anal. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68. Found: C, 57.05; H, 8.98.

The crude acetylated product (0.30 g) from **1c** gave pure **14c** (0.060 g) and **15c (X = OMe)** (0.12 g).

***anti*-2-Acetoxy-1-(benzyloxy)-3-cyclohexyl-3-methoxypropane (15c, X = OMe)**: a liquid; IR 1740 cm^{-1} (C═O); ^{1}H NMR δ 7.18–7.27 (m, 5 H), 5.10 (ddd, 1 H, J_{ac} = 4.1 and J_{bc} = J_{cd} = 5.1 Hz, H_c), 4.49 and 4.42 (ABdd, 2 H, J = 12.1 Hz), 3.69 (dd, 1 H, J_{ac} = 4.1 and J_{ab} = 9.8 Hz, H_a), 3.57 (dd, 1 H, J_{bc} = 5.1 and J_{ab} = 9.8 Hz, H_b), 3.34 (s, 3 H), 3.08 (dd, 1 H, J_{cd} = J_{ce} = 5.1 Hz, H_c), 2.01 (s, 3 H). Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.06; H, 8.52.

***anti*-3-Acetoxy-1-(benzyloxy)-3-cyclohexyl-2-methoxypropane (14c, X = OMe)**: a liquid; IR 1740 cm^{-1}; ^{1}H NMR δ 7.19–7.28 (m, 5 H), 4.88–4.94 (m, 1 H), 4.52 and 4.43 (ABdd, 2 H, J = 12.0 Hz), 3.45–3.50 (m, 1 H), 3.33–3.44 (m, 2 H), 3.36 (s, 3 H), 1.94 (s, 3 H). Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.57; H, 9.09.

The crude acetylated product (0.27 g) from **1d** gave pure ***anti*-3-acetoxy-1-(benzyloxy)-2-methoxy-4,4-dimethylpentane (14d, X = OMe)**: 0.16 g; a liquid; IR 1735 cm^{-1} (C═O); ^{1}H NMR δ 7.18–7.30 (m, 5 H), 4.85 (d, 1 H, J_{cd} = 4.2 Hz, H_d), 4.51 and 4.41 (ABdd, 2 H, J = 12.0 Hz), 3.62 (dd, 1 H, J_{ab} = 10.4 and J_{ac} = 2.2 Hz, H_a), 3.56 (dd, 1 H, J_{ab} = 10.4 and J_{bc} = 6.2 Hz, H_b), 3.49 (ddd, 1 H, J_{ac} = 2.2, J_{bc} = 6.2 and J_{cd} = 4.2 Hz, H_c), 3.35 (s, 3 H), 1.94

(s, 3 H), 0.89 (s, 9 H). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.71; H, 8.59.

The crude acetylated product (0.24 g) from **2** gave pure ***syn*-2-acetoxy-1-(benzyloxy)-3-methoxyhexane (19, X = OMe)**: 0.12 g; a liquid; IR 1735 cm^{-1} (C=O); ^{1}H NMR δ 7.22–7.36 (m, 5 H), 5.15 (ddd, 1 H, J_{ac} = 6.2, J_{bc} = 4.9 and J_{cd} = 4.0 Hz, H$_c$), 4.57 and 4.49 (ABdd, 2 H, J = 12.1 Hz), 3.66 (dd, 1 H, J_{ac} = 6.2 and J_{ab} = 10.2 Hz, H$_a$), 3.57 (dd, 1 H, J_{ab} = 10.2 and J_{bc} = 4.9 Hz, H$_b$), 3.52 (m, 1 H, H$_d$), 3.41 (s, 3 H), 2.10 (s, 3 H), 1.20–1.61 (m, 4 H), 0.91 (t, 3 H, J = 7.1 Hz). Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.62. Found: C, 68.19; H, 8.75.

Regioisomer 18 (X = OMe): ^{1}H NMR δ 7.22–7.36 (m, 5 H), 5.07 (m, 1 H), 4.61–4.64 (m, 2 H), 3.45–3.55 (m, 3 H), 3.50 (s, 3 H), 2.03 (s, 3 H).

Reaction of Epoxides 1a–d and 2 with MeONa in Anhydrous MeOH. General Procedure. The epoxide (1.0 mmol) was added to a solution of 2.5 M MeONa in anhydrous MeOH (25 mL), and the reaction mixture was refluxed for 16 h. Dilution with water, extraction with ether, and evaporation of the washed (water) ether extracts afforded a crude oily residue which was acetylated and then analyzed by GC and ^{1}H NMR to give the results shown in Tables I and II.

Methanolysis of Epoxides 1a–d and 2 in the Presence of a Metal Salt. General Procedure. The epoxide (1.0 mmol) was added to a 10 M (LiClO$_4$) or 1 M [Mg(ClO$_4$)$_2$] methanolic solution (2 mL), and the reaction mixture was heated for the time and at the temperature shown in Tables I and II. Dilution with ether and evaporation of the washed (water) ether solution afforded a crude product which was acetylated than analyzed by GC and ^{1}H NMR to give the results shown in Tables I and II.

The crude acetylated product (0.28 g) from **1d** gave pure **14d** (X = OMe) (0.14 g) and ***anti*-2-acetoxy-1-(benzyloxy)-3-methoxy-4,4-dimethylpentane (15d, X = OMe)**: 0.020 g; a liquid; IR 1738 cm^{-1} (C=O); ^{1}H NMR δ 7.18–7.30 (m, 5 H), 5.21 (ddd, 1 H, J_{ac} = J_{cd} = 4.4 and J_{bc} = 5.8 Hz, H$_c$), 4.56 and 4.53 (ABdd, 2 H, J = 12.2 Hz), 3.62 (d, 1 H, J_{cd} = 4.4 Hz, H$_d$), 3.42 (s, 3 H), 2.00 (s, 3 H), 0.87 (s, 9 H). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.68; H, 9.15.

Azidolysis of Epoxides 1a–d and 2 with NaN$_3$/NH$_4$Cl. General Procedure. Following a previously described procedure,[7] treatment of the epoxide (1.0 mmol) in a 8:1 MeOH/H$_2$O mixture (4.5 mL) with NH$_4$Cl (0.108 g, 2.0 mmol) and NaN$_3$ (0.30 g, 4.6 mmol) at 80 °C for the time shown in Tables I and II afforded a crude oily product which was acetylated then analyzed by GC and ^{1}H NMR.

The crude acetylated product (0.28 g) from **1a** gave pure ***anti*-2-acetoxy-3-azido-1-(benzyloxy)hexane (15a, X = N$_3$)**: 0.18 g; a liquid; IR 1742 cm^{-1} (C=O); ^{1}H NMR δ 7.25–7.36 (m, 5 H), 5.05 (ddd, 1 H, J_{ac} = J_{cd} = 4.1 and J_{bc} = 5.4 Hz, H$_c$), 4.56 and 4.52 (ABdd, 2 H, J = 9.1 Hz), 3.69 (dd, 1 H, J_{ab} = 10.8, and J_{ac} = 4.1 Hz, H$_a$), 3.60 (dd, 1 H, J_{ab} = 10.8 and J_{bc} = 5.4 Hz, H$_b$), 3.62–3.67 (m, 1 H), 2.10 (s, 3 H), 1.25–1.52 (m, 4 H), 0.94 (t, 3 H, J = 6.8 Hz). Anal. Calcd for $C_{15}H_{21}N_3O_3$: C, 61.83; H, 7.25; N, 14.42. Found: C, 61.70; H, 7.34; N, 14.01.

Regioisomer 14a (X = N$_3$): ^{1}H NMR δ 4.97 (m, 1 H), 4.45 (m, 2 H), 3.45–3.70 (m, 3 H), 2.06 (s, 3 H).

The crude acetylated product (0.22 g) from **1b** gave pure ***anti*-1,2-diacetoxy-3-azidohexane (15b, X = N$_3$, R$_2$ = Ac)**: 0.14 g; a liquid; IR 1740 cm^{-1} (C=O); ^{1}H NMR (CD$_3$COCD$_3$) δ 5.04 (ddd, 1 H, J_{ac} = 3.3, J_{bc} = 7.1 and J_{cd} = 4.9 Hz, H$_c$), 4.28 (dd, 1 H, J_{ac} = 3.3, J_{ab} = 12.1 Hz, H$_a$), 4.08 (dd, 1 H, J_{bc} = 7.1 and J_{ab} = 12.1 Hz, H$_b$), 3.69 (m, 1 H), 2.02 (s, 3 H), 1.97 (s, 3 H), 1.21–1.53 (m, 4 H), 1.06 (t, 3 H, J = 6.7 Hz). Anal. Calcd for $C_{10}H_{17}N_3O_4$: C, 49.37; H, 7.04; N, 17.27. Found: C, 49.52; H, 7.35; N, 16.94.

Regioisomer 14b (X = N$_3$, R$_2$ = Ac): ^{1}H NMR δ 4.96 (m, 1 H, H$_d$), 4.21 and 4.05 (ABdd, 2 H, J = 11.6 Hz), 3.89 (m, 1 H, H$_c$), 2.00 (s, 3 H), 1.98 (s, 3 H), 1.33–1.61 (m, 4 H).

The crude acetylated product (0.33 g) from **1c** gave pure ***anti*-2-acetoxy-3-azido-1-(benzyloxy)-3-cyclohexylpropane (15c, X = N$_3$)**: 0.15 g; a liquid; IR 1740 cm^{-1} (C=O); ^{1}H NMR δ 7.27–7.37 (m, 5 H), 5.15 (ddd, 1 H, J_{ac} = 5.1, J_{bc} = 3.4 and J_{cd} = 6.2 Hz, H$_c$), 4.60 and 4.53 (ABdd, 2 H, J = 12.0 Hz), 3.69 (dd, 1 H, J_{ac} = 5.1 and J_{ab} = 16.1 Hz, H$_a$), 3.47 (dd, 1 H, J_{bc} = 3.4 and J_{ab} = 16.1 Hz, H$_b$), 3.51 (dd, 1 H, J_{cd} = 6.2 and J_{de} = 7.1 Hz, H$_d$), 2.10 (s, 3 H). Anal. Calcd for $C_{18}H_{25}N_3O_3$: C, 65.23; H, 7.61; N, 12.69. Found: C, 65.01; H, 7.32; N, 12.39.

Regioisomer 14c (X = N$_3$): ^{1}H NMR δ 4.84 (m, 1 H), 4.56 (m, 2 H), 3.70 (m, 2 H), 3.54 (m, 1 H), 2.04 (s, 3 H).

The crude acetylated product (0.30 g) from **1d** gave pure ***anti*-3-acetoxy-2-azido-1-(benzyloxy)-4,4-dimethylpentane (14d, X = N$_3$)**: 0.25 g; a liquid; IR 1738 cm^{-1} (C=O); ^{1}H NMR δ 7.27–7.37 (m, 5 H), 4.79 (d, 1 H, J_{cd} = 5.3 Hz, H$_d$), 4.63 and 4.54 (ABdd, 2 H, J = 11.6 Hz), 3.65–3.78 (m, 3 H), 2.04 (s, 3 H), 0.96 (s, 9 H). Anal. Calcd for $C_{16}H_{23}N_3O_3$: C, 62.93; H, 7.59; N, 13.76. Found: C, 63.10; H, 7.45; N, 14.05.

The crude acetylated product (0.27 g) from **2** gave pure ***syn*-2-acetoxy-3-azido-1-(benzyloxy)hexane (19, X = N$_3$)**: 0.14 g; a liquid; IR 1740 cm^{-1} (C=O); ^{1}H NMR δ 7.26–7.39 (m, 5 H), 5.05 (q, 1 H, J = 5.1 Hz, H$_c$), 4.58 and 4.48 (ABdd, 2 H, J = 12.0 Hz), 3.59–3.70 (m, 1 H), 3.63 (dd, 1 H, J_{ab} = 10.3 and J_{ac} = 5.1 Hz, H$_a$), 3.61 (dd, 1 H, J_{ab} = 10.3 and J_{bc} = 5.1 Hz, H$_b$), 2.11 (s, 3 H), 1.21–1.64 (m, 4 H), 0.93 (t, 3 H, J = 6.8 Hz). Anal. Calcd for $C_{15}H_{21}N_3O_3$: C, 61.83; H, 7.25; N, 14.42. Found: C, 61.59; H, 7.64; N, 14.31.

Regioisomer 18 (X = N$_3$): ^{1}H NMR δ 4.93–5.01 (m, 1 H), 4.45–4.61 (m, 2 H), 3.71–3.80 (m, 1 H), 3.56–3.70 (m, 2 H), 2.04 (s, 3 H).

Azidolysis of Epoxides 1a–d and 2 with NaN$_3$ in the Presence of a Metal Salt. Following a previously described procedure,[4c] a solution of the epoxide (1.0 mmol) in anhydrous acetonitrile (diglyme was used in the case of epoxide **1d**) (5.0 mL) containing the metal salt (for molar concentration see Tables I and II) was stirred at 80 °C (at 120 °C in the case of **1d**) for the time shown in Tables I and II. Usual workup[4c] afforded a crude reaction product which was acetylated and then analyzed by GC and ^{1}H NMR [in the case of the reaction of **1d**, the high-boiling solvent was removed at 25 °C (0.1 mmHg)].

The crude reaction product (0.28 g) from **1d** gave **14d (X = N$_3$)** (0.12 g) and ***anti*-2-acetoxy-3-azido-1-(benzyloxy)-4,4-dimethylpentane (15d, X = N$_3$)**: 0.080 g; a liquid; IR 1740 cm^{-1} (C=O); ^{1}H NMR δ 7.27–7.37 (m, 5 H), 5.11–5.21 (m, 1 H, H$_c$), 4.60 and 4.53 (ABdd, 2 H, J = 11.6 Hz), 3.65–3.78 (m, 3 H), 2.10 (s, 3 H), 0.97 (s, 9 H). Anal. Calcd for $C_{16}H_{23}N_3O_3$: C, 62.93; H, 7.59; N, 13.76. Found: C, 62.63; H, 7.81; N, 14.01.

Aminolysis of Epoxides 1a–d and 2 with NHEt$_2$ in EtOH. General Procedure. A solution of the epoxide (1.0 mmol) in EtOH (4 mL) was treated with NHEt$_2$ (1.0 mL, 10.0 mmol), and the reaction mixture was heated under stirring at 80 °C for the time shown in Tables I and II. Usual workup[4c] afforded a crude reaction product which was acetylated then analyzed by GC and ^{1}H NMR. In the case of epoxide **1d**, no opening products were found and the unreacted epoxide was completely recovered from the crude reaction mixture.

The crude acetylated product (0.31 g) from **1a** gave pure **14a** (0.020 g) and **15a (X = NEt$_2$)** (0.16 g).

***anti*-2-Acetoxy-1-(benzyloxy)-3-(diethylamino)hexane (15a, X = NEt$_2$)**: a liquid; IR 1740 cm^{-1}; ^{1}H NMR δ 7.25–7.35 (m, 5 H), 5.13 (ddd, 1 H, J_{ac} = 4.4, J_{bc} = 5.8 and J_{cd} = 7.5 Hz, H$_c$), 4.56 and 4.49 (ABdd, 2 H, J = 12.9 Hz), 3.65 (dd, 1 H, J_{ab} = 10.4 and J_{ac} = 4.4 Hz, H$_a$), 3.58 (dd, 1 H, J_{ab} = 10.4 and J_{bc} = 5.8 Hz, H$_b$), 2.50 (m, 4 H), 2.84 (m, 1 H, H$_d$), 2.06 (s, 3 H), 1.25–1.59 (m, 4 H), 0.97 (t, 6 H, J = 7.1 Hz), 0.88 (t, 3 H, J = 7.0 Hz). Anal. Calcd for $C_{19}H_{31}NO_3$: C, 70.99; H, 9.72; N, 4.36. Found: C, 71.16; H, 9.52; N, 4.70.

***anti*-3-Acetoxy-1-(benzyloxy)-2-(diethylamino)hexane (14a, X = NEt$_2$)**: a liquid; IR 1740 cm^{-1} (C=O); ^{1}H NMR δ 7.20–7.37 (m, 5 H), 5.15 (ddd, 1 H, J = 4.3, 5.8, and 7.1 Hz, H$_d$), 4.56 and 4.49 (ABdd, 2 H, J = 13.0 Hz), 3.42–3.52 (m, 2 H), 2.94 (m, 1 H), 2.50 (m, 4 H), 1.97 (s, 3 H), 1.26–1.56 (m, 4 H), 0.95 (t, 6 H, J = 6.9 Hz), 0.91 (t, 3 H, J = 6.9 Hz). Anal. Calcd for $C_{19}H_{31}NO_3$: C, 70.99; H, 9.72; N, 4.36. Found: C, 71.25; H, 9.94; N, 4.25.

The crude acetylated product (0.26 g) from **1b** gave pure **14b** (0.025 g) and **15b (X = NEt$_2$, R$_2$ = Ac)** (0.14 g).

***anti*-1,3-Diacetoxy-2-(diethylamino)hexane (14b, X = NEt$_2$, R$_2$ = Ac)**: a liquid; IR 1740 cm^{-1} (C=O); ^{1}H NMR δ 5.05 (m, 1 H, H$_d$), 4.26 (dd, 1 H, J_{ac} = 6.4 and J_{ab} = 11.7 Hz, H$_a$), 3.92 (dd, 1 H, J_{bc} = 6.3 and J_{ab} = 11.7 Hz, H$_b$), 2.91–3.00 (m, 1 H, H$_d$), 2.51 (q, 4 H, J = 7.3 Hz), 2.07 (s, 3 H), 2.03 (s, 3 H), 1.24–1.58 (m, 4 H), 1.00 (t, 6 H, J = 7.3 Hz), 0.88 (t, 3 H, J = 6.5 Hz). Anal. Calcd for $C_{14}H_{27}NO_4$: C, 61.51; H, 9.95; N, 5.12. Found: C, 61.87; H, 10.15; N, 5.32.

***anti*-1,2-Diacetoxy-3-(diethylamino)hexane (15b, X = NEt_2, R_2 = Ac)**: a liquid; IR 1743 cm^{-1} (C═O); ^1H NMR δ 5.10 (ddd, 1 H, $J_{ac} = 2.3$, $J_{bc} = 6.6$ and $J_{cd} = 8.7$ Hz, H_c), 4.46 (dd, 1 H, $J_{ac} = 2.3$ and $J_{ab} = 11.8$ Hz, H_a), 4.40 (dd, 1 H, $J_{bc} = 6.6$ and $J_{ab} = 11.8$ Hz, H_b), 2.85 (m, 1 H, H_d), 2.51 (q, 4 H, $J = 7.3$ Hz), 2.06 (s, 3 H), 2.04 (s, 3 H), 1.22–1.61 (m, 4 H), 1.00 (t, 6 H, $J = 7.3$ Hz), 0.89 (t, 3 H, $J = 6.7$ Hz). Anal. Calcd for $C_{14}H_{27}NO_4$: C, 61.51; H, 9.95; N, 5.12. Found: C, 61.40; H, 10.17; N, 5.41.

The crude acetylated product (0.35 g) from **1c** gave pure ***anti*-2-acetoxy-1-(benzyloxy)-3-cyclohexyl-3-(diethylamino)propane (15c, X = NEt_2)**: 0.21 g; a liquid; IR 1740 cm^{-1} (C═O); ^1H NMR δ 7.26–7.34 (m, 5 H), 5.32 (ddd, 1 H, $J_{ac} = 4.6$ and $J_{bc} = J_{cd} = 6.3$ Hz, H_c), 4.55 and 4.49 (ABdd, 2 H, $J = 12.7$ Hz), 3.62 (dd, 1 H, $J_{ab} = 8.6$ and $J_{ac} = 4.6$ Hz, H_a), 3.58 (dd, 1 H, $J_{ab} = 8.6$ and $J_{bc} = 6.3$ Hz, H_b), 2.70 (dd, 1 H, $J_{cd} = J_{de} = 6.3$ Hz, H_d), 2.50–2.47 (m, 4 H), 2.07 (s, 3 H), 0.88 (t, 6 H, $J = 7.1$ Hz). Anal. Calcd for $C_{22}H_{35}NO_3$: C, 73.10; H, 9.75; N, 3.87. Found: C, 73.31; H, 9.46; N, 4.09.

Regioisomer **14c (X = NEt_2)**: ^1H NMR δ 4.86 (dd, 1 H, J = 3.7 and 7.9 Hz, H_d), 4.38 (s, 2 H), 3.40–3.56 (m, 2 H), 2.46–2.57 (m, 1 H), 2.49 (m, 4 H), 1.90 (s, 3 H), 0.94 (t, 6 H, $J = 7.1$ Hz).

The crude acetylated product (0.30 g) from **2** gave pure **18** (0.030 g) and **19 (X = NEt_2)** (0.18 g).

***syn*-2-Acetoxy-1-(benzyloxy)-3-(diethylamino)hexane (19, X = NEt_2)**: a liquid; IR 1740 cm^{-1} (C═O); ^1H NMR δ 7.26–7.34 (m, 5 H), 5.15 (ddd, 1 H, $J_{ac} = 4.4$ and $J_{cd} = J_{bc} = 5.7$ Hz, H_c), 4.59 and 4.45 (ABdd, 2 H, $J = 12.1$ Hz), 3.64 (dd, 1 H, $J_{ab} = 10.7$ and $J_{ac} = 4.4$ Hz, H_a), 3.61 (dd, 1 H, $J_{ab} = 10.7$ and $J_{bc} = 5.7$ Hz, H_b), 2.85 (m, 1 H, H_d), 2.61 (six lines, 2 H, J = 7.2 and 13.0 Hz), 2.45 (six lines, 2 H, J = 6.9 and 13.3 Hz), 2.07 (s, 3 H), 1.21–1.43 (m, 4 H), 0.97 (t, 6 H, $J = 7.1$ Hz), 0.88 (t, 3 H, $J = 6.6$ Hz). Anal. Calcd for $C_{19}H_{31}NO_3$: C, 70.99; H, 9.72; N, 4.36. Found: C, 71.30; H, 9.49; N, 4.65.

***syn*-3-Acetoxy-1-(benzyloxy)-2-(diethylamino)hexane (18, X = NEt_2)**: a liquid; IR 1740 cm^{-1} (C═O); ^1H NMR δ 7.24–7.35 (m, 5 H), 5.12 (m, 1 H), 4.46 (s, 2 H), 3.46–3.66 (m, 2 H), 2.83 (m, 1 H), 2.50 (q, 4 H, $J = 6.7$ Hz), 2.02 (s, 3 H), 1.20–1.58 (m, 4 H), 0.97 (t, 6 H, $J = 6.7$ Hz), 0.90 (t, 3 H, $J = 7.0$ Hz). Anal. Calcd for $C_{19}H_{31}NO_3$: C, 70.99; H, 9.72; N, 4.36. Found: C, 70.81; H, 9.84; N, 4.74.

Aminolysis of Epoxides 1a–d and 2 with $NHEt_2$ in the Presence of $LiClO_4$. General Procedure. Following a previously described procedure,[4c] a solution of the epoxide (1.0 mmol) in anhydrous acetonitrile (2.0 mL) was treated with $LiClO_4$ (1.07 g, 10.0 mmol) and $NHEt_2$ (1.0 mL, 10.0 mmol), and the reaction mixture was stirred at the temperature and for the time shown in Tables I and II. Usual workup[4c] afforded a crude reaction product which was acetylated then analyzed by GC and ^1H NMR to give the results shown in Tables I and II.

The crude acetylated product (0.31 g) from **1d** gave pure ***anti*-3-acetoxy-1-(benzyloxy)-2-(diethylamino)-4,4-dimethylpentane (14d, X = NEt_2)**: 0.15 g; a liquid; IR 1740 cm^{-1} (C═O); ^1H NMR δ 7.29–7.42 (m, 5 H), 4.87 (d, 1 H, $J_{cd} = 4.4$ Hz, H_d), 4.54 and 4.46 (ABdd, 2 H, $J = 12.1$ Hz), 3.47–3.58 (m, 2 H), 3.21 (ddd, 1 H, $J_{ac} = J_{bc} = 5.8$ and $J_{cd} = 4.4$ Hz, H_c), 2.59–2.57 (m, 4 H), 1.99 (s, 3 H), 1.04 (t, 6 H, $J = 7.1$ Hz), 0.94 (s, 9 H). Anal. Calcd for $C_{20}H_{33}NO_3$: C, 71.60; H, 9.91; N, 4.17. Found: C, 71.92; H, 9.87; N, 4.29.