Regiochemical Control of the Ring Opening of Aziridines by Means of Chelating Processes. Synthesis and Ring-Opening Reactions of *cis*- and *trans*-Aziridines Derived from 4-(Benzyloxy)cyclohexene

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The regiochemical outcome of the ring opening of aziridines bearing a polar remote functionality was verified in a conformationally semirigid bicyclic system in which the polar functionality (OBn) is in an homoallylic relationship to the aziridine ring. The couples of diastereoisomeric unactivated *cis*-**3** and *trans*-**4** and activated aziridines *cis*-**5** and -**7** and *trans*-**6** and -**8** derived from 4-(benzyloxy)-cyclohexene were prepared, and some of their opening reactions were studied. The regioselectivity observed in the opening reactions of the cis derivatives turned out to depend largely on the opening (standard, strongly acidic, or metal-assisted) reaction conditions, thus providing a nice regioalternating process. The results obtained are rationalized by admitting the incursion of chelate bidentate intermediate structures in which the proton or the metal is actively involved.

The nucleophilic ring opening of small-membered heterocyclic compounds such as oxiranes and aziridines can play an important role in modern synthetic chemistry, particularly when 1,2-difunctional compounds are needed. While the stereochemistry of the nucleophilic addition of the above-mentioned heterocyclic systems is usually completely anti,[1-3] the control of the regioselectivity of the addition process in simple unsymmetrically substituted systems is not so univocal.

In previous papers, we demonstrated the possibility of controlling the regioselectivity of the addition to 1,2-epoxides possessing polar remote functionalities by metal ion-assisted processes.[4] The best results were obtained with the conformationally semirigid cyclic 1,2-epoxides **1** and **2** bearing a benzyloxy group (OBn) as the remote polar heterofunctionality in the β-position.[4a-c] In the case of the cis derivative **1**, the appropriate use of nonchelating or metal-assisted chelating procedures leads to a practically complete control of the regioselectivity, thus affording regioalternating processes.[4a-c] We now want to evaluate the possibility of obtaining control of the regioselectivity also in the ring opening of aziridines by means of the presence of a polar functionality (OBn) of the same type as previously used with the oxiranes.[4] For this reason, we prepared and studied the *cis*-**3** and the *trans*-aziridine **4**, structurally corresponding to the epoxide *cis*-**1** and *trans*-**2**, respectively. We also prepared and studied the corresponding activated[3] aziridines **5**–**8**, which bear a strong electron-withdrawing group on the nitrogen, such as the ethoxycarbonyl (COOEt) in **5** and **6** or the tosyl group (Ts) in **7** and **8**, respectively. Actually, the activated aziridines **5**–**8** were expected to be more reactive than the unactivated ones, **3** and **4**, toward nucleophiles, under any reaction conditions.[3]

1	X=O	**2**
3	X=NH	**4**
5	X=NCOOEt	**6**
7	X=NTs	**8**

Results

The stereospecific synthesis of the pair of diastereoisomeric aziridines **3** and **4** was effected from the epoxides **2** and **1**,[4b] respectively, by reaction of the corresponding 1,2-azido alcohols[4c] with triphenylphosphine (PPh_3) and the intermediate formation of 1,3,2-oxazaphospholidines (Scheme 1).[5]

While the *cis*-epoxide **1** was obtained in a nice stereoselective way from the corresponding olefin **12**, as previously described,[4b] the trans isomer **2** could only be obtained in relatively small amounts by (a somewhat difficult) flash chromatography of the almost equimolar mixture of the *cis*-**1** and *trans*-epoxide **2** obtained by epoxidation of the olefin **12** with *m*-CPBA.[4b] Looking for an easier synthesis of the trans isomer **2**, we tried to take advantage of the much higher reactivity of the *cis*-epoxide **1** with respect to the trans one **2**, as a result of the ability of the cis isomer **1** to react by chelation processes.[4a-c] Actually, when an equimolar mixture of **1** and **2** was left in contact with $(CH_3)_2CuLi$ at −78 °C for 40 min, the *cis*-epoxide **1** reacted completely to give the corresponding opening product, the methyl alcohol **9**,[4a] while the trans isomer **2** did not react in these conditions and was recovered almost unchanged. Simple flash chromatog-

[⊗] Abstract published in *Advance ACS Abstracts,* April 1, 1995.

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

(3) (a) Deyrup, J. A. In *Small Ring Heterocycles, Part 1*; Hassner, A., Ed.; Interscience: New York, 1983; p 1. (b) Tanner, D. *Angew.Chem. Int. Ed. Engl.* **1994**, *33*, 599, and references therein.

(4) (a) Chini, M.; Crotti, P.; Flippin, L. A.; Macchia, F. *Tetrahedron Lett.* **1989**, *30*, 653. (b) *J. Org.Chem.* **1990**, *55* , 4265. (c) *Ibid.* **1991**, *56*, 7043. (d) Chini, M.; Crotti, P.; Flippin, L. A.; Macchia, F.; Pineschi, M. *J. Org.Chem.* **1992**, *57*, 1405. (e) Chini, M.; Crotti, P.; Flippin, L. A.; Gardelli, C.; Macchia, F. *J. Org.Chem.* **1992**, *57*, 1713. (f) Chini, M.; Crotti, P.; Flippin, L. A.; Gardelli, C.; Giovani, E.; Macchia, F.; Pineschi, M. *J. Org.Chem.* **1993**, *58* , 1221.

(5) (a) Pöchlauer, P.; Müller, E. P.; Peringer, P. *Helv. Chim. Acta* **1984**, *67*, 1238. (b) Legters, J.; Thijs, L.; Zwanenburg, B. *Tetrahedron Lett.* **1989**, *30*, 4881.

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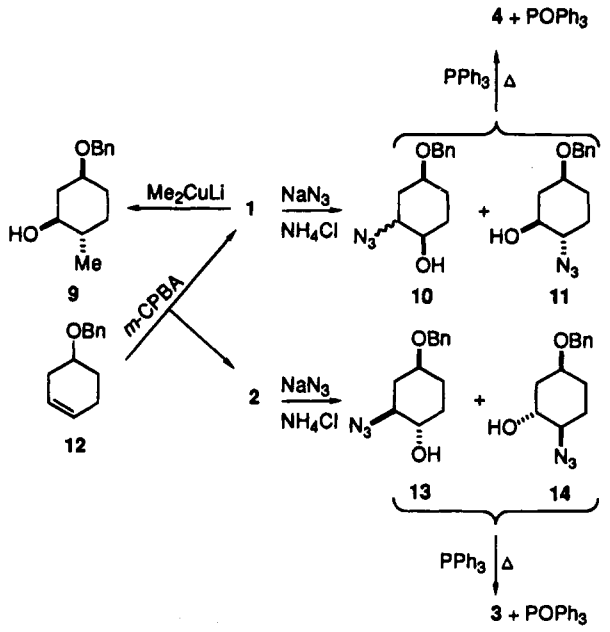
Scheme 1



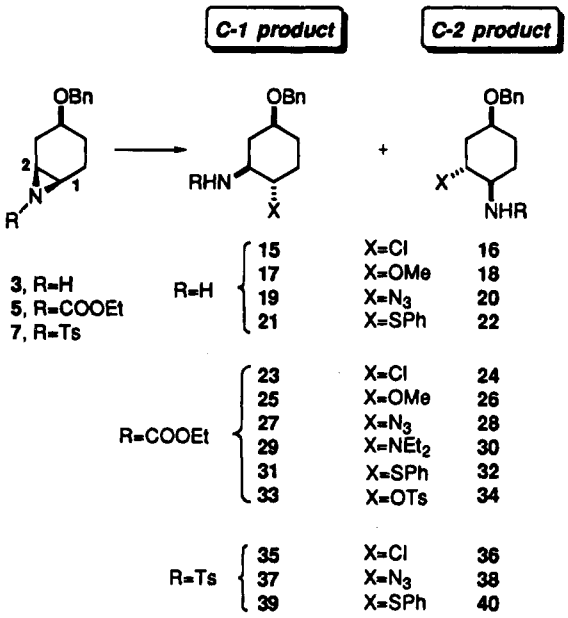
raphy of the reaction mixture yielded pure **2**, almost quantitatively.

Separate treatment of the *cis*-**1** and *trans*-**2** epoxides with NaN_3 in aqueous methanol in the presence of NH_4Cl, in accordance with the previously reported procedure,[4c] yielded the two pairs of regioisomeric azido alcohols **10** and **11**, and **13** and **14**, respectively. Heating each pair of azido alcohols in CH_3CN in the presence of PPh_3[5] yielded a crude reaction product containing the *cis*-**3** (from **13** and **14**) and the *trans*-aziridine **4** (from **10** and **11**), respectively, impure with triphenylphosphine oxide ($POPh_3$). Subsequently, aziridines **3** and **4** were obtained pure only by means of a difficult column-chromatography separation. More advantageously, the crude reaction mixture containing the aziridine (**3** or **4**) and $POPh_3$ was treated with ethyl chloroformate in the presence of Et_3N, thus converting the aziridine into the corresponding *N*-ethoxycarbonyl derivative (**5** or **6**, respectively), which was separated very easily from $POPh_3$ by flash chromatography. The *N*-substituted aziridines **5** and **6** thus obtained were quantitatively converted into the pure *N*-unsubstituted aziridines **3** and **4**, respectively, by their treatment with MeONa in MeOH at room temperature. The reaction of aziridines **3** and **4** with TsCl afforded the corresponding *N*-tosyl derivatives **7** and **8**.

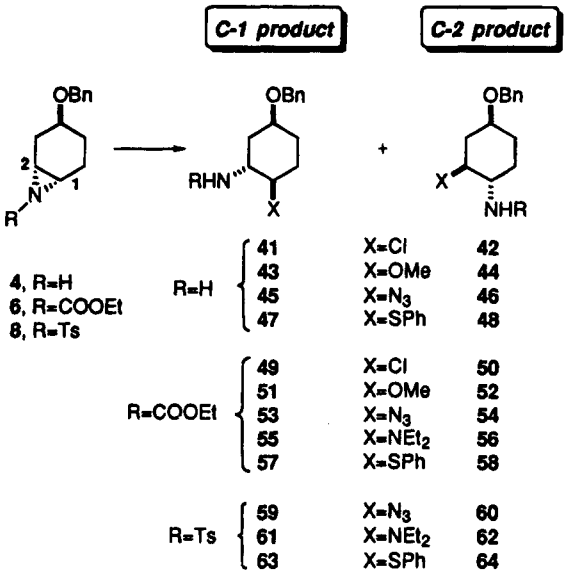
The aziridines **3**–**8** were subjected to several ring-opening reactions with different nucleophiles (Cl^-, MeOH, N_3^-, Et_2NH, PhSH) both under standard nonchelating conditions (reactions carried out under protic acid catalysis or without any catalysis) and under conditions which had proved to be useful supporting evidence of the intervention of chelated species in the reactions of the epoxides [reactions carried out in the presence of a metal salts or metallic species (chelating conditions)] (Schemes 2 and 3).[4] The determination of the relative amounts of regioisomeric addition products (*C-1* and *C-2 products*)[6] in the ring opening reactions was accomplished by ^1H NMR analysis (see below) of the crude reaction mixtures (Tables 1 and 2).

(6) The C-1 and C-2 product nomenclature refers to the attacking site of the nucleophile, *i.e.* at the C-(1) or C-(2) aziridine carbon of aziridines **3**–**8**, in accordance with the numbering scheme shown in Schemes 2 and 3.

Scheme 2



Scheme 3



The reactions of the unactivated *cis*-aziridine **3** carried out under standard conditions showed a poor regioselectivity, except for those carried out under strong acid catalysis (entries 1 and 3, Table 1) in which a discreet C-1 selectivity was observed (78–79%). The same type of selectivity was also observed under metal salt-promoted opening conditions (entries 2, 8, 9, and 11, Table 1). The reactions of the activated *cis*-aziridines **5** and **7** showed, as expected,[3] a higher reactivity than the corresponding unactivated aziridine **3**. Under nonchelating conditions, **5** and **7** showed a marked C-2 regioselectivity, which in some cases is practically complete (entries 14, 19, 21, 23, 27–29, and 31, Table 1). On the other hand, as observed to a lesser extent with the *N*-unsubstituted *cis*-aziridine **3**, but now in a more dramatic way, the use of either a strong protic or a metal ion catalysis in the opening reactions of **5** and **7** practically leads to a reversal of the regioselectivity of the nucleophilic addition, and a complete C-1 selectivity is observed in some cases (entries 12, 13, 16, 17, 20, 22, 24–26, 30, and 32, Table 1).

Table 1. Regioselectivity of the Ring Opening Reactions of the Cis Aziridines 3, 5, and 7 under Standard and Chelating Conditions

entry	aziridine	reagents[a]	solvent	reaction time and temp	C-1 product (regioselect.)	C-2 product (regioselect.)	yield, %
1	**3**	HCl	$CHCl_3$	10 min (rt)	**15** (79)	**16** (21)	98
2	**3**	$TiCl_4$	THF	1 h (−78 °C)	(74)	(26)	25
3	**3**	$MeOH/H_2SO_4$	MeOH	18 h (rt)	**17** (78)	**18** (22)	80
4	**3**	MeONa	MeOH	5 d (70 °C)	no reaction		
5	**3**	NaN_3/NH_4Cl	$MeOH:H_2O$ 8:1	5 h (60 °C)	**19** (70)	**20** (30)	95
6	**3**	NaN_3/H_2SO_4	acetone	18 h (rt)	(47)	(53)	30
7	**3**	NaN_3	DMSO	3 d (100 °C)	(61)	(39)	30
8	**3**	$NaN_3/Mg(ClO_4)_2$	THF	5 h (60 °C)	(78)	(22)	90
9	**3**	$NaN_3/Zn(OTf)_2$	THF	5 h (60 °C)	(87)	(13)	94
10	**3**	$PhSH/NEt_3$	MeOH	18 h (rt)	**21** (59)	**22** (41)	98
11	**3**	$PhSH/Mg(ClO_4)_2$	THF	5 h (70 °C)	(72)	(28)	98
12	**5**	HCl	$CHCl_3$	10 min (rt)	**23** (>99)	**24** (<1)	98
13	**5**	$TiCl_4$	THF	1 h (−78 °C)	(>99)	(<1)	98
14	**5**	NaCl	DMF	3 d (120 °C)	(18)	(82)	97
15	**5**	$MeOH/H_2SO_4$	MeOH	2 h (rt)	**25** (67)	**26** (33)	99
16	**5**	$MeOH/LiClO_4$ 6 M	MeOH	2 h (70 °C)	(94)	(6)	98
17	**5**	$MeOH/LiClO_4$ 16 M	MeOH	2 h (70 °C)	(>99)	(<1)	95
18	**5**	NaN_3/NH_4Cl	$MeOH:H_2O$ 8:1	2 h (80 °C)	**27** (52)	**28** (48)	95
19	**5**	NaN_3	DMF	24 h (rt)	(<1)	(>99)	94
20	**5**	$NaN_3/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(>99)	(<1)	96
21	**5**	$NHEt_2$	EtOH	24 h (80 °C)	**29** (<1)	**30** (>99)	72
22	**5**	$NHEt_2/LiClO_4$ 2 M	MeCN	24 h (rt)	(>99)	(<1)	97
23	**5**	$PhSH/NEt_3$	MeOH	18 h (rt)	**31** (<1)	**32** (>99)	92
24	**5**	$PhSH/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(>99)	(<1)	90
25	**5**	TsOH	$CHCl_3$	10 min (rt)	**33** (>99)	**34** (<1)	98
26	**7**	HCl	$CHCl_3$	10 min (rt)	**35** (>99)	**36** (<1)	98
27	**7**	NaCl	DMF	18 h (120 °C)	(<1)	(>99)	75
28	**7**	NaN_3/NH_4Cl	$MeOH:H_2O$ 8:1	2 h (80 °C)	**37** (8)	**38** (92)	96
29	**7**	NaN_3	DMF	24 h (rt)	(<1)	(>99)	94
30	**7**	$NaN_3/LiClO_4$ 5 M	MeCN	2 h (80 °C)	(85)	(15)	96
31	**7**	$PhSH/NEt_3$	MeOH	18 h (rt)	**39** (<1)	**40** (>99)	94
32	**7**	$PhSH/LiClO_4$ 5 M	MeCN	2 h (80 °C)	(81)	(19)	96

[a] 0.5 M $Mg(ClO_4)_2$ and 0.25 M $Zn(OTf)_2$.

In the addition reactions to the *trans*-aziridines **4**, **6**, and **8**, a complete C-1 selectivity was commonly found, with the only exception of the reactions with MeOH and Et_2NH (entries 3, 11, 12, 16, 17, 23, and 24, Table 2) in which substantial amounts of the regioisomeric C-2 product are formed. However, almost no differences were observed when different reaction conditions (strong protic acid catalysis, metal ion catalysis, etc.) were applied. Also in this case, the activated aziridines **6** and **8** showed a higher reactivity than the unactivated one **4**, in accordance with expectations.[3]

Discussion

A comparison of the results obtained in the opening reactions of the *cis* (**3**, **5**, and **7**) and *trans*-aziridines (**4**, **6**, and **8**), with the corresponding ones obtained with the *cis*-**1** and *trans*-epoxide **2**[4a−c] shows close analogies, but also striking dissimilarities, in some cases.

The opening reactions of the *cis*-aziridines (**3**, **5**, and **7**) showed a marked dependence of the regioselectivity on the reaction conditions, as already found for the reactions of the *cis*-epoxide **1**.[4a−c] However, in the case of epoxide **1** the reversal of selectivity (from C-2 to C-1 type) was observed only on passing from standard opening conditions (including mild or strong protic acid catalysis) to chelating ones,[4a−c] while in the case of the *cis*-aziridines (**3**, **5**, and **7**), the same type of regioselectivity reversal was observed also when a strong protic acid catalysis was used (entries 1, 12, 14, 25−27, Table 1).

The C-2 selectivity observed in the reaction of the *cis*-aziridines **3**, **5**, and **7** under standard conditions can be rationalized on the basis of the preferential diaxial attack of the nucleophiles on the more stable conformations **a** of the *cis*-aziridines (**3**, **5**, and **7**), in accordance with the Fürst−Plattner rule (Scheme 4).[4a−c,7] In these conditions, the decrease in C-2 selectivity observed on passing from the *N*-tosyl (**7**) to the *N*-ethoxycarbonyl (**5**), and then to the *N*-unsubstituted aziridine (**3**) (see, for example entries 5, 18, and 28, Table 1), could be justified by the electron-withdrawing effect of the remote benzyloxy group which makes the two secondary aziridine carbons not completely electronically equivalent and the C-(1) carbon the more reactive one. This difference between C-(1) and C-(2) carbons, though unimportant in the case of highly reactive systems such as the aziridines **5** and **7**, could become so important in the case of the less reactive *N*-unsubstituted aziridine **3**, that it is forced to react through its less stable conformation **3b**: the diaxial attack of the nucleophile on **3b** affords discreet amounts of C-1 products, as observed (Table 1).

The complete or almost complete C-1 selectivity observed in the reactions of the *cis*-aziridines **3**, **5**, and **7** in the presence of metal ions can be explained, as in the case of the *cis*-epoxide **1**,[4a−c] by invoking the formation of an intermediate chelated structure of type **67** ($Y = M^+$) which can be formed by an initial coordination of the metal with the oxygen of the benzyloxy group of the aziridine, either in conformation **a** or **b** (structures **65** and **66**, respectively), followed by an entropically favored further coordination with the aziridine nitrogen (Scheme 4). The axial attack of the nucleophile on **67** ($Y = M^+$),

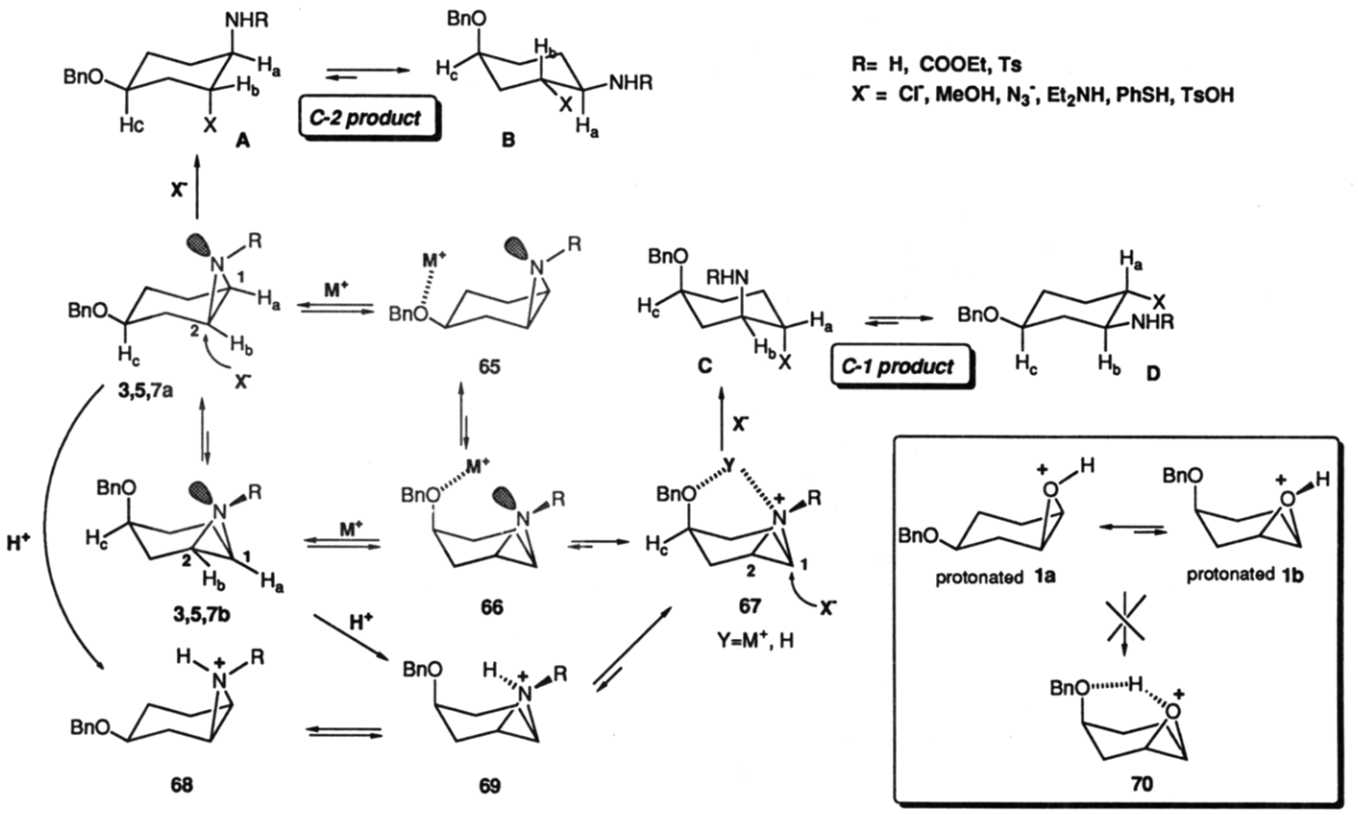
(7) (a) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Interscience: New York, 1965; p 102. (b) Fürst, A.; Plattner, P. A. *Abstract of Papers*, 12th International Congress of Pure and Applied Chemistry, 1951; p 409.

Table 2. Regioselectivity of the Ring Opening Reactions of the Trans Aziridines 4, 6, and 8 under Standard and Chelating Conditions

entry	aziridine	reagents[a]	solvent	reaction time and temp	C-1 product (regioselect.)	C-2 product (regioselect.)	yield, %
1	**4**	HCl	$CHCl_3$	10 min (rt)	**41** (>99)	**42** (<1)	70
2	**4**	$TiCl_4$	THF	1 h (−78 °C)	(>99)	(<1)	20
3	**4**	$MeOH/H_2SO_4$	MeOH	18 h (rt)	**43** (81)	**44** (19)	96
4	**4**	MeONa	MeOH	5 d (70 °C)	no reaction		
5	**4**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	5 h (60 °C)	**45** (>99)	**46** (<1)	98
6	**4**	$NaN_3/Mg(ClO_4)_2$	THF	5 h (60 °C)	(>99)	(<1)	90
7	**4**	$PhSH/NEt_3$	MeOH	18 h (rt)	**47** (>99)	**48** (<1)	97
8	**4**	$PhSH/Mg(ClO_4)_2$	THF	5 h (70 °C)	(>99)	(<1)	96
9	**6**	HCl	$CHCl_3$	10 min (rt)	**49** (>99)	**50** (<1)	98
10	**6**	NaCl	DMF	3 d (120 °C)	(62)	(38)	60
11	**6**	$MeOH/H_2SO_4$	MeOH	2 h (rt)	**51** (67)	**52** (33)	95
12	**6**	MeOH/$LiClO_4$ 6 M	MeOH	2 h (70 °C)	(52)	(48)	90
13	**6**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	3 h (80 °C)	**53** (>99)	**54** (<1)	95
14	**6**	NaN_3	DMF	24 h (rt)	(>99)	(<1)	50
15	**6**	$NaN_3/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(>99)	(<1)	60
16	**6**	$NHEt_2$	EtOH	4 d (80 °C)	**55** (32)	**56** (68)	80
17	**6**	$NHEt_2/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(41)	(59)	92
18	**6**	$PhSH/NEt_3$	MeOH	18 h (rt)	**57** (>99)	**58** (<1)	93
19	**6**	$PhSH/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(>99)	(<1)	91
20	**8**	NaN_3/NH_4Cl	MeOH:H_2O 8:1	2 h (80 °C)	**59** (>99)	**60** (<1)	96
21	**8**	NaN_3	DMF	24 h (rt)	(>99)	(<1)	94
22	**8**	$NaN_3/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(>99)	(<1)	96
23	**8**	$NHEt_2$	EtOH	24 h (80 °C)	**61** (29)	**62** (71)	92
24	**8**	$NHEt_2/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(39)	(61)	95
25	**8**	$PhSH/NEt_3$	MeOH	18 h (rt)	**63** (>99)	**64** (<1)	95
26	**8**	$PhSH/LiClO_4$ 2 M	MeCN	2 h (80 °C)	(>99)	(<1)	98

[a] 0.5 M $Mg(ClO_4)_2$.

Scheme 4



in accordance with the Fürst–Plattner rule[4a–c,7] and with all the stereoelectronic factors implicated in the chelation-controlled ring opening of small heterocycles,[4,8] leads mainly to C-1 products, as actually found (Table 1).

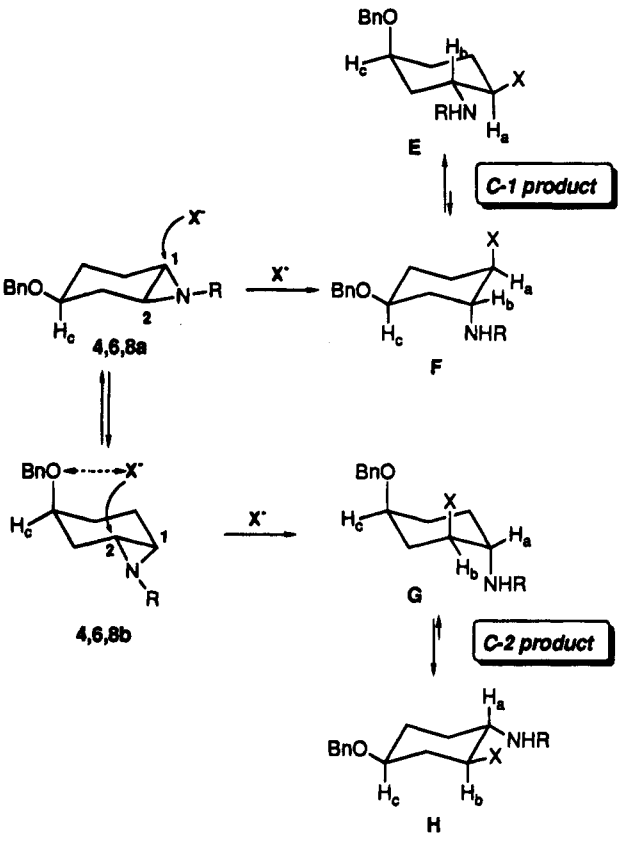
However, unlike the behavior of the corresponding *cis*-epoxide **1**,[4a–c] the cis aziridines **3**, **5**, and **7** exhibit a dramatic change in selectivity also when a strong protic acid catalysis is used, leading, as in the case of the metal ion-catalyzed reactions, to a complete or nearly complete C-1 selectivity (Table 1). In order to explain this result, it is necessary to hypothesize a mechanistic scheme, analogous to the one admitted for the metal ion-catalyzed reactions, implying a chelate species of type **67** in which the M^+ group is in the present case the proton itself (**67**, Y = H). In this rationalization, the proton initially links

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

to the basic nitrogen of the aziridine (see below), either in conformation **a** or **b**, to give the corresponding species **68** and **69**, respectively, with the added proton reasonably inside the cyclohexyl moiety because of the preference of the R substituent for the less hindered outside region of the ring.[9] In this position, the proton can easily further coordinate to the benzyloxy oxygen by a hydrogen bond, thus generating the intermediate structure **67** (Y = H). The axial attack of the nucleophiles on **67** (Y = H) affords C-1 products, as experimentally observed. Experimental confirmation of this mechanistic hypothesis is given by an ^{1}H NMR experiment carried out with the *N*-unsubstituted *cis*-aziridine **3**. When a $CDCl_3$ solution of **3** is treated at rt with increasing amounts of *p*-toluenesulfonic acid (TsOH) (up to a small equimolar excess, see Experimental Section), the half-bandwidth value ($W_{1/2}$)[10] of the signal of the methine proton (H_c) α to the benzyloxy group decreases from 26 to 12.5 Hz, indicating a dramatic change in the conformational equilibrium, from the initially preferred conformation **a** to the final conformation **b**, reasonably due to the formation of a hydrogen-bonded stabilized structure such as **67** (Y = H) (Scheme 4). Unfortunately, attempts to carry out the same experiment with the *N*-substituted aziridine **5** lead, even at low temperatures (<−20 °C), to the corresponding opening addition product, in which the low nucleophilic TsOH is found to be added to the aziridine ring (compound **33**, Scheme 2; entry 25, Table 1). However, the regiochemistry of the addition product **33** is also in this case consistent with a C-1 product, in accordance with the intermediate formation of a chelated structure of type **67** (Y = H). On the contrary, the addition of TsOH to a $CDCl_3$ solution of the *N*-unsubstituted *trans*-aziridine **4** does not provide evidence (^{1}H NMR, see Experimental Section) of any change in the conformational equilibrium. It is not easy to offer a complete explanation for the different behavior of the *cis*-epoxide **1**[4b,c] and of the *cis*-aziridines **3**, **5**, and **7** under strong protic acid catalysis. One explanation could be tentatively postulated by admitting that, unlike **3**, **5** and **7**, in the reaction of **1** the protonation occurs from the less hindered outside part of the cyclohexyl ring, as shown in the protonated conformers **1a** and **1b** (Scheme 4), that is in a position in which coordination with the heterofunctionality (OBn) is not possible. Moreover, the presence in **67** (Y = H) from aziridines **3**, **5** and **7** of an N−H−O interaction stronger than the O−H−O interaction present in **70**, if formed, from epoxide **1**, could constitute a further contributory cause of the different behavior observed between aziridines **3**, **5**, and **7** and epoxide **1** under strong acid conditions (Scheme 4).

The aziridines **3** and **4** are particularly unreactive under basic conditions, and attempts to obtain their reaction under strong base catalysis (MeO^- in MeOH) were usuccessful; on the other hand, when the same reaction conditions were used with the *N*-substituted aziridines **5** and **6**, their easy conversion into the *N*-unsubstituted aziridines **3** and **4**, respectively, was observed. In view of the stability under the same alkaline conditions of all the opening products (urethanes) obtained in the opening reactions of **5** and **6**, the result obtained with activated aziridines **5** and **6** is the consequence of the mostly pyramidal nature, in contrast with common amides, of the nitrogen in these compounds (aziridines **5** and **6**), with the *N*-substituent further from the cyclohexyl moiety.[11,12]

Scheme 5



R= H, COOEt, Ts
X⁻ = Cl⁻, MeOH, N_3^-, Et_2NH, PhSH

In the trans derivatives, a very close analogy has been observed between the reactions of the aziridines **4**, **6**, and **8** and those of the corresponding epoxide **2**,[4a-c] as regards both the chemical behavior under different reaction conditions and the regioselectivity. As no coordination by a metal or a proton is possible for structural reasons between the heterofunctionalities present in the molecule of trans derivatives, all the aziridines examined (**4**, **6**, and **8**) give practically the same regiochemical result independently of the reaction conditions (Table 2). The formation of both C-1 and C-2 products in the methanolysis and the aminolysis with Et_2NH of the *trans*-aziridines **4**, **6**, and **8**, carried out under standard conditions, can be rationalized on the basis of a diaxial attack[7] of the nucleophile on both the nearly equivalent conformations **a** and **b** of the starting aziridines (Scheme 5). On the contrary, the complete C-1 selectivity observed in the reactions of **4**, **6**, and **8** with nucleophiles such as N_3^-, Cl^-, PhS^- (the actual nucleophile in the PhSH/Et_3N opening conditions) and PhSH (the actual nucleophile under PhSH/$LiClO_4$ opening conditions) (Table 2) points to a preferential reactivity of these aziridines in their conformation **a**. Evidently, in these conditions, the diaxial ring-opening process of aziridines **4**, **6**, and **8** in

(9) This statement is superfluous in the case of aziridine **3** (R = H), where structure **69** (R = H) (Scheme 4) is obviously the only possible one.

(10) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: London, 1969; p 286.

(11) Reference 3a, p 8.

(12) (a) Zacharis, H. M.; Trefonas, L. M. *J. Heterocycl. Chem.* **1970**, *7*, 755. (b) *Ibid.* **1968**, *5*, 343. (c) Trefonas, L. M.; Majeste, R. *J. Heterocycl. Chem.* **1965**, *2*, 80.

their conformation **b** is largely precluded by the unfavorable interaction between the negatively charged nucleophile (in the case of N_3^-, Cl^-, and PhS^-), or the large sulfur (in the case of PhSH) and the oxygen of the benzyloxy group, as shown in Scheme 5.

In conclusion, the appropriate use of standard, or metal-assisted chelating reaction conditions, together with the interesting behavior observed in the opening reactions of the *cis*-aziridines **3**, **5**, and **7** under strong protic acid catalysis leads to a practically complete regiocontrol of the addition, thus providing a synthetically useful regioalternating process.[4a]

Structures, Configurations, and Conformations

The relative configurations of the *cis*-(**3**, **5**, and **7**) and *trans*-aziridines (**4**, **6**, and **8**) are unequivocally demonstrated on the basis of their stereospecific methods of synthesis from the known *trans*-**2** and *cis*-epoxide **1**,[4a-c] respectively. As the pairs of azido alcohols **10** and **11**, and **13** and **14**, are formed from the corresponding epoxides **1** and **2** with a complete inversion of the configuration, the cyclohexane carbon bearing the azide group in these compounds has the opposite configuration with respect to the starting epoxide.[4c] On the other hand, in the conversion of each pair **10** and **11**, and **13** and **14**, into the aziridines **4** and **3**, respectively, the configuration of that carbon remains unchanged, thus fixing also the relative configuration of the aziridines **3** and **4**. The configuration of the *N*-substituted *cis*-**5** and -**7** and *trans*-**6** and -**8** aziridines, is clearly defined by their preparation from the corresponding *N*-unsubstituted ones **3** and **4**. The conformational equilibria of the aziridines **3**–**8** (see Schemes 4 and 5) were confirmed by examination of the $W_{1/2}$ value[10] of the H_c proton α to the OBn group, in the ^1H NMR spectra of these compounds (Table 3). In the cis derivatives **3**, **5**, and **7** the $W_{1/2}$ value (26 Hz for **3** and **5**, and 28 Hz for **7**) indicate the conformer **a** with the benzyloxy group equatorial as the most stable conformer, very likely due to the repulsive interactions of the aziridine nitrogen and the benzyloxy oxygen present in the alternative conformer **b** (Scheme 4). On the other hand, the lower $W_{1/2}$ values observed for proton H_c in the *trans*-aziridines **4**, **6**, and **8** (15 Hz for **4**, 13 Hz for **6**, and 14 Hz for **8**) suggest for these compounds an almost equimolar conformational equilibrium between conformer **a** and **b** (Scheme 5).[10]

The trans relationship between the X and NHR groups in both the C-1 and the C-2 products from either the *cis*-(**3**, **5**, and **7**) or the *trans*-aziridines (**4**, **6**, and **8**) can be assumed on the basis of the usual anti stereoselectivity commonly observed in the ring opening of these systems.[1-4] On the other hand the cis and trans relationship between the benzyloxy and the NHR group in all the ring-opening products must necessarily be the same as in the starting aziridines. The regiochemical assignment within the pairs of C-1 and the C-2 products from the *cis*- (**3**, **5**, and **7**) and the *trans*-aziridines (**4**, **6**, and **8**) were carried out by means both of the $W_{1/2}$ value[10] of the signals of protons α to NHR, X, and OBn groups (protons H_a, H_b, and H_c, Schemes 4 and 5) in the ^1H NMR spectra of these compounds (Table 3) and by simple conformational considerations. In the case of the C-1 and C-2 products from the *cis*-aziridines (**3**, **5**, and **7**), the relatively large $W_{1/2}$ value of the signals of the protons H_a, H_b, and H_c observed for one regioisomer are consistent with a C-1 product structure, which should exist in the reasonably more stable triequatorial conformation **D** (Scheme 4). On the other hand, the large $W_{1/2}$ value of the signal of the protons H_a and H_b and the much lower $W_{1/2}$ value of the signal of the proton H_c observed for the other regioisomer strongly indicate for this compound the alternative C-2 product structure which exists mainly in the conformation **B** with the OBn group axial (Scheme 4). However, in some cases, due to a noncomplete separation of the signals of protons H_a–H_c or to a not-so-evident difference of their $W_{1/2}$ values, some appropriate chemical correlations were carried out in order to get further confirmation of the regiochemical assignment. For example, the C-1 and C-2 products obtained in the reactions of the *N*-substituted *cis*-aziridine **5** with methanol (X = OCH_3), azide ion (X = N_3), and thiophenol (X = SPh) (compounds **25**–**28** and **31**–**32**, Scheme 2) were deprotected, by

Table 3. ^1H NMR Data for Aziridines 3–8 and Opening Products 15–63

	^1H NMR, δ		
compd	H_a ($W_{1/2}$, Hz)[a,b]	H_b ($W_{1/2}$, Hz)[a,b]	H_c ($W_{1/2}$, Hz)[c]
3	*d*	*d*	3.39 (26.0)[e]
4	*d*	*d*	3.47 (15.5)[e]
5	*d*	*d*	3.28 (26.0)[e]
6	*d*	*d*	3.53 (13.0)[e]
7	*d*	*d*	3.28 (28.0)[e]
8	*d*	*d*	3.21 (14.0)[f]
15	*d*	2.76 (26.0)[a,g]	*d*
16	2.73 (28.0)[a,e]	3.94 (28.0)[b,g]	3.76 (9.0)[e]
17	2.82 (26.5)[b,g]	2.63 (26.5)[a,g]	*d*
18	2.65 (26.0)[a,e]	3.20 (26.0)[b,e]	3.80 (10.8)[e]
19	3.02 (26.0)[b,e]	2.55 (26.0)[a,g]	3.43 (23.5)[e]
20	2.56 (26.4)[a,h]	3.39 (26.4)[b,g]	3.82 (7.5)[e]
21	*d*	*d*	3.38 (25.7)[e]
22	2.64 (25.8)[a,e]	3.19 (26.9)[b,e]	3.56 (8.6)[e]
23	*d*	3.88 (17.5)[a,e]	3.71 (12.0)[e]
24	3.63 (23.5)[a,e]	*d*	3.76 (11.8)[e]
25	3.27 (23.0)[b,e]	3.81 (15.2)[a,e]	3.72 (15.2)[e]
26	3.60 (26)[a,e]	3.36 (20)[b,e]	3.77 (13.0)[e]
27	*d*	*d*	*d*
28	*d*	*d*	3.79 (8.8)[e]
29	2.97 (22.9)[b,e]	*d*	*d*
30	3.30 (23.8)[a,e]	2.97 (28.0)[b,e]	3.80 (8.0)[e]
31	3.33 (17.4)[b,e]	3.79 (17.4)[a,e]	3.63 (13.0)[e]
32	3.50 (26.6)[a,e]	3.34 (26.6)[b,h]	3.67 (11.0)[e]
33	4.50 (25.0)[b,e]	*d*	*d*
35	4.21 (9.0)[b,e]	3.53 (14.0)[a,i]	3.67 (10.0)[e]
36	3.34 (29.0)[a,e]	5.06 (27.0)[b,h]	3.75 (9.0)[e]
37	*d*	3.24 (16.0)[a,i]	*d*
38	2.94 (25.0)[a,e]	3.40 (25.0)[b,e]	3.65 (8.5)[e]
39	*d*	*d*	3.59 (10.0)[f]
40	2.96 (21.5)[a,i]	2.98 (23.5)[b,h]	3.53 (12.1)[e]
41	3.60 (24.0)[b,h]	3.17 (27.0)[a,g]	3.86 (8.5)[e]
43	3.10 (25.4)[b,e]	2.90 (25.4)[a,h]	3.72 (7.8)[e]
44	*d*	2.84 (27.0)[b,g]	*d*
45	*d*	*d*	3.72 (7.3)[e]
47	2.72 (27.9)[b,h]	3.06 (27.9)[a,h]	3.75 (9.3)[e]
49	*d*	*d*	3.72 (9.0)[e]
50	*d*	*d*	*d*
51	3.04 (22.0)[b,h]	3.76 (26.0)[a,e]	3.56 (11.4)[e]
52	*d*	2.99 (27.0)[b,h]	*d*
53	3.23 (26.9)[b,e]	3.72 (>23.0)[a,e]	*d*
55	2.94 (22.0)[b,e]	*d*	*d*
56	*d*	*d*	*d*
57	3.06 (26.7)[b,e]	3.85 (27.0)[a,e]	3.69 (8.9)[e]
59	3.09 (24.0)[b,i]	3.27 (27.0)[a,e]	3.53 (8.0)[e]
61	*d*	3.09 (26.0)[a,h]	3.69 (7.6)[e]
62	2.64 (21.5)[a,h]	*d*	3.31 (21.5)[g]
63	2.99 (23.0)[b,h]	3.34 (23.5)[a,i]	3.64 (12.3)[e]

Compounds **34**, **42**, **46**, **48**, **54**, **58**, **60**, and **64**, which are not present in the opening reactions of the corresponding aziridine, are not included. [a] C*H*NHR (C*H*NR in the case of aziridines **3**–**8**). [b] C*H*X. [c] C*H*OBn (see Schemes 2–5). [d] The signal overlaps with other signals. [e] Multiplet. [f] Quintet. [g] Doublet of doublets of doublets. [h] Doublet of doublets of doublets. [i] Sextet.

heating at 100 °C with a 1 M KOH solution in ethylene glycol,[13] to give the same products (compounds **17**–**22**, Scheme 2) obtained in the corresponding reactions of the *N*-unsubstituted aziridine **3**. Alternatively, the C-1 product obtained by addition of the chloride ion to the *N*-unsubstituted *cis*-aziridine **3** (compound **15**) was transformed into the *N*-ethoxycarbonyl (**23**) and *N*-tosyl derivatives (**35**) by its simple reaction with ClCOOEt and TsCl, respectively.

The same considerations were used in order to distinguish between the C-1 and C-2 products (existing mainly in the conformation **E** and **H**, respectively, Scheme 5) obtained in the ring-opening reactions of the *trans*-aziridines **4**, **6**, and **8**. However, in this case the regiochemical assignment was slightly simplified by the fact that the C-1 product is often the only reaction product and, as a consequence, no chemical correlations were necessary.

Experimental Section

For general experimental details, see ref 4b–f. Olefin **12**, *cis*-epoxide **1**, and the 46:54 mixture of epoxides *cis*-**1** and *trans*-**2**, obtained in the *m*-CPBA oxidation of **12**, were prepared as previously described.[4b]

Kinetic Separation of *trans*-Epoxide 2. A suspension of CuI (9.86 g, 0.052 mol) in anhyd Et_2O (70 mL) was treated at −15 °C with 1.6 M MeLi in Et_2O (65 mL), and the resulting mixture was stirred for 20 min at the same temperature. After cooling at −78 °C, a 46:54 mixture of epoxides **1** and **2** (6.04 g, 0.029 mmol) in anhyd Et_2O (60 mL) was slowly added to the reaction mixture. The proceeding reaction was monitored by GC: after 40 min at −78 °C the *cis*-epoxide **1** was no longer present in the reaction mixture. Saturated aqueous NH_4Cl was added, and stirring was prolonged for 30 min, allowing the reaction temperature to equilibrate to rt. Evaporation of the washed (saturated aqueous NaCl) ether solution afforded a liquid product consisting of an almost 1:1 mixture of the *trans*-epoxide **2** and the methyl alcohol **9**[4a] (GC and ^1H NMR) which were separated by flash chromatography (an 8:2 mixture of hexane and AcOEt was used as the eluant) to give pure epoxide **2** (2.11 g, 70% yield) and methyl alcohol **9** (2.90 g).[4a]

Reaction of Epoxides 1 and 2 with NaN_3–NH_4Cl. General procedure. Proceeding as previously described,[4c] treatment of a solution of the epoxide (2.04 g, 10.0 mmol) in an 8:1 MeOH/H_2O mixture (24 mL) with NaN_3 (3.02 g, 46.5 mmol) in the presence of NH_4Cl (0.99 g, 18.5 mmol) for 18 h at 70 °C afforded a crude reaction product consisting of a mixture of the corresponding azido alcohols **10** and **11** (96:4) (2.39 g) from epoxide **1**, and **13** and **14** (5:95) (2.34 g) from epoxide **2**.[4c]

Synthesis of Aziridines 3 and 4. The following procedure is typical. A mixture of the azido alcohols **13** and **14** (2.47 g, 10.0 mmol) in CH_3CN (10 mL) was treated with triphenylphosphine (PPh_3) (2.62 g, 10.0 mmol), and the resulting solution was stirred at rt until the evolution of N_2 was observed (30 min) and then refluxed overnight.[5] After cooling, the solvent was removed under vacuum (rotating evaporator), and the residue was repeatedly extracted with petroleum ether. Evaporation of the organic extracts afforded an oily residue (2.13 g) consisting of a mixture of aziridine **3**, PPh_3, and triphenylphosphine oxide ($POPh_3$) which was subjected to flash chromatography (a 6:2:2 mixture of hexane, $CHCl_3$, and Et_3N was used as the eluant) to yield pure **(1β,3β,6β)-3-(benzyloxy)-7-azabicyclo[4.1.0]heptane** (**3**) (1.62 g, 80% yield), as a liquid: ^1H NMR δ 7.22–7.37 (m, 5H), 4.50 and 4.45 (ABdd, 2H, J = 12.0 Hz), 3.28–3.51 (m, 1H), 2.17–2.37 (m, 1H), 1.97–2.17 (m, 3H), 1.70–1.91 (m, 2H), 1.36–1.70 (m, 2H), and see Table 3. ^{13}C NMR δ 139.41, 129.03, 128.15, 74.50, 70.56, 31.29, 30.12, 29.23, 24.82, 23.52. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.84; H, 8.42; N, 6.88. Found: C, 76.95; H, 8.51; N, 6.69.

Analogous treatment of a mixture of azido alcohols **10** and **11** (2.47 g, 10.0 mmol) with PPh_3 (2.62 g, 10.0 mmol) afforded pure **(1α,3β,6α)-3-(benzyloxy)-7-azabicyclo[4.1.0]heptane** (**4**) (1.70 g, 84% yield), as a liquid: ^1H NMR δ 7.10–7.40 (m, 5H), 4.51 and 4.44 (ABdd, 2H, J = 11.8 Hz), 3.38–3.56 (m, 1H), 1.97–2.31 (m, 4H), 1.66–1.97 (m, 2H), 1.33–1.66 (m, 2H), and see Table 3. ^{13}C NMR δ 139.41, 128.79, 127.96, 127.87, 72.12, 70.36, 31.33, 29.47, 25.08, 21.64. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.84; H, 8.42; N, 6.88. Found: C, 76.74; H, 8.51; N, 6.78.

Treatment of Aziridines 3 and 4 with *p*-Toluenesulfonic Acid in $CDCl_3$. The following procedure is typical. A solution of the *cis*-aziridine **3** (0.020 g, 0.1 mmol) in $CDCl_3$ (0.5 mL) in a NMR tube was treated with increasing amounts of *p*-toluenesulfonic acid monohydrate (TsOH). The contemporary ^1H NMR examination of the half-bandwidth value ($W_{1/2}$) of the signal of the proton H_c (Scheme 4) gave the following results: added TsOH = 0 mmol, $W_{1/2}$ (H_c) = 26 Hz; TsOH = 0.066 mol, $W_{1/2}$ (H_c) =14.6 Hz; TsOH = 0.1 mmol, $W_{1/2}$ (H_c) = 13.8 Hz; TsOH = 0.12 mmol, $W_{1/2}$ (H_c) = 12.5 Hz.

The same procedure on trans azide **4** (Scheme 5) gave the following results: added TsOH = 0 mmol, $W_{1/2}$ (H_c) = 15.5 Hz; TsOH = 0.066 mol, $W_{1/2}$ (H_c) = 11.5 Hz; TsOH = 0.1 mmol, $W_{1/2}$ (H_c) = 11.5 Hz; TsOH = 0.12 mmol, $W_{1/2}$ (H_c) = 11.5 Hz.

Synthesis of Aziridines 5 and 6. The following procedure is typical. A solution of aziridine **3** (1.42 g, 6.7 mmol) in anhyd Et_2O (20 mL) containing Et_3N (1.2 mL, 8.4 mmol) was treated at 0 °C with a solution of ethyl chloroformate (0.911 g, 8.4 mmol) in anhyd Et_2O (5 mL), and the reaction mixture was stirred at 0 °C for 1 h. Evaporation of the filtered organic solution afforded pure **(1β,3β,6β)-3-(benzyloxy)-7-(ethoxycarbonyl)-7-azabicyclo[4.1.0]heptane** (**5**) (1.78 g, 97% yield), as a liquid: IR 1718 cm^{-1} (CO); ^1H NMR δ 7.14–7.40 (m, 5H), 4.49 (s, 2H), 4.12 (q, 2H, J = 7.1 Hz), 3.19–3.38 (m, 1H), 2.53–2.66 (m, 2H), 2.13–2.47 (m, 2H), 1.60–1.90 (m, 3H), 1.38–1.59 (m, 1H), 1.26 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 164.39, 139.26, 128.93, 128.03, 74.12, 70.34, 62.88, 37.81, 36.02, 30.66, 24.82, 29.19, 14.92. Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.81; H, 7.54; N, 5.23.

Analogous treatment of aziridine **4** (1.42 g, 6.7 mmol) with ethyl chloroformate (0.91 g, 8.4 mmol) afforded pure **(1α,3β,6α)-3-(benzyloxy)-7-(ethoxycarbonyl)-7-azabicyclo[4.1.0]heptane** (**6**) (1.76 g, 95% yield), as a solid, mp 24.5–26.5 °C: IR 1724 cm^{-1} (CO); ^1H NMR δ 7.20–7.40 (m, 5H), 4.51 and 4.44 (ABdd, 2H, J = 11.9 Hz), 4.13 (q, 2H, J = 7.1 Hz), 3.47–3.60 (m, 1H), 2.62–2.74 (m, 2H), 2.19 (dd, 1H, J = 15.0 and 4.7 Hz), 1.83–2.10 (m, 3H), 1.50–1.65 (m, 2H), 1.27 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 164.39, 139.21, 128.81, 127.91, 127.87, 127.25, 71.23, 70.33, 62.72, 37.47, 36.58, 30.19, 24.28, 20.32, 14.80. Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 70.05; H, 7.72; N, 5.01.

Deprotection of Aziridines 5 and 6. The following procedure is typical. A solution of aziridine **5** (2.75 g, 10.0 mmol) in a 1.5 M MeONa solution in anhyd MeOH (20 mL) was stirred at rt for 18 h. After concentration of the solution (rotating evaporator), the residue was taken up in ether; evaporation of the washed (saturated aqueous NaCl) ether solution afforded pure aziridine **3** (1.99 g, 98% yield).

The same procedure on **6** (2.75 g) afforded pure aziridine **4** (2.0 g, 98% yield).

Purification of Aziridines 3 and 4 through the Corresponding Derivatives 5 and 6. The following procedure is typical. The mixture of aziridine **3**, PPh_3, and $POPh_3$ (1.90 g, containing about 78% of **3**), obtained in the reaction of the azido alcohols **13** and **14** with PPh_3 (see above), was treated with ethyl chloroformate (1.19 g, 11.0 mmol) in the presence of Et_3N (1.53 mL, 11.0 mmol) following the procedure described above, to give a crude reaction product (2.83 g) which was subjected to flash chromatography. Elution with a 3:1 mixture of hexane and AcOEt afforded pure aziridine **5** (1.87 g). Treatment of **5** (1.87 g) with 1.5 M MeONa in anhyd MeOH (14 mL), following the procedure described above, afforded pure aziridine **3** (1.4 g, 94% overall yield).

(13) Wenkert, E.; Hudlicky, T; Showalter, H. D. H. *J. Am. Chem. Soc.* **1978**, *100*, 4893.

Analogous treatment of the mixture of aziridine **4**, PPh_3, and $POPh_3$ (1.90 g) afforded pure aziridine **4** (1.38 g, 93% overall yield).

Synthesis of Aziridines 7 and 8. The following procedure is typical. A solution of aziridine **3** (0.61 g, 3.0 mmol) in anhyd pyridine (3.0 mL) was treated at 0 °C with TsCl (0.63 g, 3.3 mmol), and the reaction mixture was maintained at the same temperature for 1 h and then 24 h at −20 °C. Dilution with ether, and evaporation of the washed (saturated aqueous $CuSO_4$ and saturated aqueous NaCl) organic solution afforded pure **(1β,3β,6β)-3-(benzyloxy)-7-tosyl-7-azabicyclo[4.1.0]-heptane** (**7**) (0.90 g, 84% yield), as a solid, mp 95−97 °C (from hexane): ^{1}H NMR δ 7.81 (d, 2H, J = 8.2 Hz), 7.14−7.40 (m, 7H), 4.49 and 4.44 (ABdd, 2H, J = 12.1 Hz), 3.18−3.38 (m, 1H), 2.84−3.04 (m, 2H), 2.44 (s, 3H), 2.24−2.44 (m, 1H), 2.01−2.18 (m, 1H), 1.33−1.85 (m, 4H), and see Table 3. ^{13}C NMR δ 144.90, 139.10, 136.49, 131.31, 128.26, 128.15, 128.07, 73.66, 70.65, 40.19, 39.38, 29.73, 24.74, 23.58, 22.30. Anal. Calcd for $C_{20}H_{23}NO_3S$: C, 67.20; H, 6.48; N, 3.92. Found: C, 67.43; H, 6.59; N, 4.09.

Analogous treatment of aziridine **4** (0.6 g) with TsCl afforded pure **(1α,3β,6α)-3-(benzyloxy)-7-tosyl-7-azabicyclo[4.1.0]-heptane** (**8**) (0.96 g, 90% yield), as a solid, mp 76.5−77.5 °C (from hexane): ^{1}H NMR δ 7.80 (d, 2H, J = 8.2 Hz), 7.18−7.40 (m, 7H), 4.46 and 4.40 (ABdd, 2H, J = 11.0 Hz), 3.21 (quintet, 1H, J = 4.5 Hz), 2.95−3.06 (m, 2H), 2.43 (s, 3H), 1.91−2.18 (m, 3H), 1.68−1.88 (m, 1H), 1.48−1.65 (m, 2H), and see Table 3. ^{13}C NMR δ 144.84, 139.10, 135.93, 130.26, 128.99, 128.26, 128.15, 128.00, 70.72, 70.51, 40.42, 39.44, 29.30, 23.93, 22.23, 19.42. Anal. Calcd for $C_{20}H_{23}NO_3S$: C, 67.20; H, 6.48; N, 3.92. Found: C, 67.35; H, 6.54; N, 3.89.

Reaction of Aziridines 3−7 with HCl-$CHCl_3$. General procedure. A solution of the aziridine (0.50 mmol) in $CHCl_3$ (3.0 mL) was treated with 36% aqueous HCl (2.0 mL), and the reaction mixture was stirred vigorously for 10 min at rt. In the case of aziridines **3** and **4**, the organic solution was separated and the aqueous solution was basified with saturated aqueous NH_3. Extraction with ether and evaporation of the combined ether extracts afforded an oily residue which was analyzed by ^{1}H NMR (Tables 1 and 2). In the case of aziridines **5**, **6**, and **7** the $CHCl_3$ solution was separated, washed (saturated aqueous $NaHCO_3$), and evaporated to give an oily residue consisting of the corresponding chloro derivatives (^{1}H NMR, see Schemes 2 and 3 and Tables 1 and 2).

The crude reaction product (0.12 g) from the aziridine **3** was subjected to semipreparative TLC (a 6:2:2 mixture of hexane, $CHCl_3$ and Et_3N was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **16**) afforded pure chloro amines **15** (0.090 g) and **16** (0.021 g).

***t*-2-Amino-*t*-4-(benzyloxy)-*r*-1-chlorocyclohexane** (**15**), as a solid, mp 54−55 °C (from hexane): ^{1}H NMR δ 7.14−7.45 (m, 5H), 4.54 (s, 2H), 3.34−3.64 (m, 2H), 2.73 (dddd, 1H, J = 11.3, 9.5 and 4.0 Hz), 2.00−2.48 (m, 3H), 1.15−1.74 (m, 3H), and see Table 3. ^{13}C NMR δ 139.04, 128.98, 128.19, 128.09, 75.42, 70.89, 68.05, 55.87, 39.98, 32.76, 31.93. Anal. Calcd for $C_{13}H_{18}ClNO$: C, 65.12; H, 7.57; N, 5.84. Found: C, 65.24; H, 7.81; N, 5.92.

***c*-4-(Benzyloxy)-*t*-2-chloro-*r*-1-aminocyclohexane** (**16**), as a liquid: ^{1}H NMR δ 7.20−7.42 (m, 5H), 4.51 and 4.37 (ABdd, 2H, J = 11.9 Hz), 3.97 (dddd, 1H, J = 11.9, 9.6 and 4.2 Hz), 3.70−3.82 (m, 1H), 2.62−2.83 (m, 1H), 2.49 (dddd, 1H, J = 13.6, 6.5 and 3.5 Hz), 1.92−2.11 (m, 1H), 1.35−1.92 (m, 4H), and see Table 3. ^{13}C NMR δ 139.15, 129.07, 128.21, 128.06, 74.12, 70.65, 65.59, 57.84, 40.36, 29.15, 28.88. Anal. Calcd for $C_{13}H_{18}ClNO$: C, 65.12; H, 7.57; N, 5.84. Found: C, 65.19; H, 7.77; N, 5.71.

Proceeding as above, the reaction of **3** was repeated also with an HCl-saturated ether solution to give a completely similar result.

The crude reaction product (0.115 g) from aziridine **4** was subjected to semipreparative TLC (a 6:2:2 mixture of hexane, $CHCl_3$ and Et_3N was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-amino-*c*-4-(benzyloxy)-*r*-1-chlorocyclohexane** (**41**) (0.080 g), as a liquid: ^{1}H NMR δ 7.10−7.40 (m, 5H), 4.50 (s, 2H), 3.70−3.81 (m, 1H), 3.60 (ddd, 1H, J = 10.1 and 5.3 Hz), 3.17 (dddd, 1H, J = 11.5, 9.8 and 4.2 Hz), 2.18−2.34 (m, 1H), 1.91−2.18 (m, 3H), 1.20−1.54 (m, 2H), and see Table 3. ^{13}C NMR δ 139.26, 129.01, 128.15, 128.00, 73.02, 70.62, 68.86, 52.98, 38.63, 30.83, 30.17. Anal. Calcd for $C_{13}H_{18}ClNO$: C, 65.12; H, 7.57; N, 5.84. Found: C, 65.31; H, 7.69; N, 5.79.

The crude solid reaction product (0.153 g) from aziridine **5** was recrystallized from hexane to give pure ***t*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-chlorocyclohexane** (**23**) (0.105 g), as a solid, mp 64−66 °C: IR 1690 cm^{-1} (CO); ^{1}H NMR δ 7.21−7.41 (m, 5H), 5.91−6.10 (m, 1H), 4.58 and 4.50 (ABdd, 2H, J = 11.8 Hz), 3.99−4.21 (m, 3H), 3.70−3.97 (m, 1H), 3.63−3.79 (m, 1H), 2.17−2.43 (m, 2H), 1.83−2.08 (m, 1H), 1.60−1.85 (m, 3H), 1.24 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.42, 138.77, 128.18, 128.42, 128.12, 74.13, 71.17, 61.50, 60.03, 52.55, 31.51, 26.23, 25.74, 15.27. Anal. Calcd for $C_{16}H_{22}ClNO_3$: C, 61.63; H, 7.11; N, 4.49. Found: C, 61.37; H, 7.29; N, 4.31. Compound **23** was prepared also by reaction of the chloro amine **15** with ethyl chloroformate, following the procedure described above.

The crude solid reaction product (0.15 g) from aziridine **6** was recrystallized from hexane to give pure ***c*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-chlorocyclohexane** (**49**) (0.11 g), as a solid, mp 93−94 °C: IR 1688 cm^{-1} (CO); ^{1}H NMR δ 7.21−7.40 (m, 5H), 5.00−5.28 (m, 1H), 4.55 and 4.49 (ABdd, 2H, J = 11.9 Hz), 4.13 (q, 2H, J = 7.1 Hz), 3.78−4.01 (m, 2H), 3.66−3.78 (m, 1H), 2.33−2.50 (m, 1H),1.88−2.30 (m, 3H), 1.37−1.70 (m, 2H), 1.25 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.65, 139.12, 129.01, 128.15, 128.09, 72.64, 70.50, 62.48, 61.52, 53.36, 36.38, 31.03, 29.76, 15.21. Anal. Calcd for $C_{16}H_{22}ClNO_3$: C, 61.63; H, 7.11; N, 4.49. Found: C, 61.54; H, 7.01; N, 4.67.

The crude reaction product (0.194 g) from aziridine **7** consisted of ***t*-4-(benzyloxy)-*t*-2-(tosylamino)-*r*-1-chlorocyclohexane** (**35**), as a semisolid: ^{1}H NMR δ 7.69 (d, 2H, J = 8.3 Hz), 7.19−7.48 (m, 7H), 6.29 (d, 1H, J = 7.8 Hz), 4.56 and 4.40 (ABdd, 2H, J = 12.0 Hz), 4.15−4.27 (m, 1H), 3.61−3.74 (m, 1H), 3.53 (sextet, 1H, J = 3.9 Hz), 2.43 (s, 3H), 2.33−2.43 (m, 1H), 2.05 (ddd, 1H, J = 14.6 and 3.6 Hz), 1.56−1.91 (m, 3H), 1.34−1.50 (m, 1H) and see Table 3. ^{13}C NMR δ 144.03, 138.57, 138.41, 130.40, 129.30, 128.62, 128.06, 127.58, 73.92, 71.29, 60.26, 54.36, 29.65, 24.27, 23.68, 22.23. Anal. Calcd for $C_{20}H_{24}ClNO_3S$: C, 60.98; H, 6.14; N, 3.55. Found: C, 60.81; H, 6.36; N, 3.79. Compound **35** was prepared also by reaction of the chloro amine **15** with TsCl, following the procedure described above.

Reaction of Aziridines 3−5 with $TiCl_4$. General procedure. A solution of the aziridine (0.25 mmol) in anhyd CH_2Cl_2 (5 mL) was treated at −78 °C with 1 M $TiCl_4$ in CH_2Cl_2 (0.3 mL), and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was basified with 36% aqueous NH_3: evaporation of the washed (saturated aqueous NaCl) organic solution afforded a crude reaction product which was analyzed by ^{1}H NMR (Tables 1 and 2).

Reaction of Aziridines 5−7 with NaCl−DMF. General procedure. A solution of the aziridine (0.50 mmol) in DMF (4 mL) containing NaCl (0.87 g, 15.0 mmol) was stirred at 120 °C for 3 days (18 h in the case of **7**). Dilution with ether and evaporation of the washed (saturated aqueous NaCl) organic solution afforded a crude reaction product which was analyzed by ^{1}H NMR (Tables 1 and 2).

The crude reaction product (0.151 g) from aziridine **5** was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **23**) afforded pure **23** (0.028 g) and ***c*-4-(benzyloxy)-*t*-2-chloro-*r*-1-[(ethoxycarbonyl)amino]cyclohexane** (**24**) (0.10 g), as a liquid: IR 1697 cm^{-1} (CO); ^{1}H NMR δ 7.18−7.40 (m, 5H), 4.59 (d, 1H, J = 7.4 Hz), 4.49 and 4.46 (ABdd, 2H, J = 12.0 Hz), 3.96−4.20 (m, 1H), 4.12 (q, 2H, J = 7.1 Hz), 3.70−3.82 (m, 1H), 3.56−3.70 (m, 1H), 2.46 (dddd, 1H, J = 13.8, 4.2 and 2.2 Hz), 1.47−2.16 (m, 5H), 1.24 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 157.04, 139.03, 129.10, 128.32, 128.09, 73.60, 70.80, 61.64, 60.04, 56.53, 40.37, 28.56, 28.06, 15.24. Anal. Calcd for $C_{16}H_{22}ClNO_3$: C, 61.63; H, 7.11; N, 4.49. Found: C, 61.39; H, 6.80; N, 4.69.

The crude reaction product (0.15 g) from aziridine **6** was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **49**) afforded pure **49** (0.020 g) and ***t*-4-(benzyloxy)-*t*-2-chloro-*r*-1-[(ethoxycarbonyl)amino]cyclohexane (50)** (0.011 g), as a solid mp 121–123 °C: IR 1698 cm^{-1} (CO); ^1H NMR δ 7.14–7.44 (m, 5H), 4.63 (d, 1H, J = 9.7 Hz), 4.48 (s, 2H), 4.05 (q, 2H, J = 7.1 Hz), 3.20–3.73 (m, 3H), 2.58 (dddd, 1H, J = 12.5, 6.5 and 4.0 Hz), 1.68–1.94 (m, 2H), 1.10–1.50 (m, 3H), 1.18 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.80, 138.90, 129.15, 128.40, 128.22, 75.67, 71.10, 61.68, 60.40, 57.33, 42.57, 31.12, 30.24, 15.24. Anal. Calcd for $C_{16}H_{22}ClNO_3$: C, 61.63; H, 7.11; N, 4.49. Found: C, 61.81; H, 7.24; N, 4.31.

The crude reaction product (0.190 g) from azirdine **7** was subjected to semipreparative TLC (a 8:2 mixture of hexane and AcOEt was used as the eluant). Extraction of the most intense band afforded pure ***c*-4-(benzyloxy)-*t*-2-chloro-*r*-1-(tosylamino)cyclohexane (36)** (0.135 g), as a semisolid: ^1H NMR δ 7.74 (d, 2H, J = 8.3 Hz), 7.20–7.40 (m, 7H), 5.06 (ddd, 1H, J = 10.3 and 4.5 Hz), 4.74 (d, 1H, J = 7.9 Hz), 4.46 (s, 2H), 3.69–3.80 (m, 1H), 3.24–3.44 (m, 1H), 2.42 (s, 3H), 2.12–2.29 (m, 1H), 1.59–2.03 (m, 4H), 1.40–1.59 (m, 1H), and see Table 3. ^{13}C NMR δ 161.31, 143.95, 139.15, 138.89, 130.20, 129.07, 128.29, 128.15, 127.68, 72.79, 71.52, 70.74, 56.96, 35.37, 28.64, 28.43, 22.20. Anal. Calcd for $C_{20}H_{24}ClNO_3S$: C, 60.98; H, 6.14; N, 3.55. Found: C, 61.27; H, 6.42; N, 3.84.

Methanolysis of Aziridines 3–6 with 0.2 N H_2SO_4–MeOH. General procedure. A solution of the aziridine (0.50 mmol) in 0.2 N H_2SO_4–MeOH (5 mL) was stirred at rt for 18 h (2 h in the case of **5** and **6**). Dilution with saturated aqueous $NaHCO_3$, extraction with ether, and evaporation of the washed (water) ether extracts afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1 and 2).

The crude reaction product (0.114 g) from aziridine **3** was subjected to semipreparative TLC (an 8:1:1 mixture of hexane, $CHCl_3$, and Et_3N was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **18**) afforded pure amino ethers **17** (0.064 g) and **18** (0.016 g).

***t*-2-Amino-*t*-4-(benzyloxy)-*r*-1-methoxycyclohexane (17)**, as a liquid: ^1H NMR δ 7.18–7.40 (m, 5H), 4.54 (s, 2H), 3.28–3.52 (m, 1H), 3.38 (s, 3H), 2.82 (dddd, 1H, J = 10.3, 8.8 and 3.9 Hz), 2.63 (dddd, 1H, J = 11.5, 8.8 and 4.0 Hz), 2.01–2.34 (m, 3H), 1.00–1.45 (m, 3H), and see Table 3. ^{13}C NMR δ 139.32, 129.04, 128.18, 85.79, 75.99, 70.97, 57.39, 53.59, 39.25, 30.60, 26.32. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.45; H, 8.99; N, 5.95. Found: C, 71.31; H, 9.25; N, 6.08.

***c*-4-(Benzyloxy)-*t*-2-methoxy-*r*-1-aminocyclohexane (18)**, as a liquid: ^1H NMR δ 7.17–7.42 (m, 5H), 4.54 and 4.47 (ABdd, 2H, J = 12.0 Hz), 3.75–3.86 (m, 1H), 3.36 (s, 3H), 3.12–3.28 (m, 1H), 2.55–2.76 (m, 1H), 2.25–2.43 (m, 1H), 1.85–2.05 (m, 1H), 1.30–1.84 (m, 4H), and see Table 3. ^{13}C NMR δ 139.61, 129.04, 128.23, 128.11, 82.04, 74.38, 70.71, 57.30, 53.61, 33.86, 30.40, 28.63. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.45; H, 8.99; N, 5.95. Found: C, 71.29; H, 9.05; N, 5.79.

The crude reaction product (0.11 g) from aziridine **4** consisted of a mixture of amino ethers **43** and **44** (^1H NMR, see Table 2) which did not separate under TLC conditions. Pure **43** (0.026 g) and **44** (0.019 g) were obtained by deprotection of the corresponding urethanes **51** (0.054 g) and **52** (0.040 g), respectively (see below), followed by semipreparative TLC purification.

***t*-2-Amino-*c*-4-(benzyloxy)-*r*-1-methoxycyclohexane (43)**, as a liquid: ^1H NMR δ 7.18–7.41 (m, 5H), 4.49 (s, 2H), 3.66–3.78 (m, 1H), 3.40 (s, 3H), 3.00–3.20 (m, 1H), 2.90 (ddd, 1H, J = 9.7 and 3.6 Hz), 2.12–2.29 (m, 1H), 1.82–2.12 (m, 2H), 1.50–1.72 (m, 1H), 1.24–1.50 (m, 2H), and see Table 3. ^{13}C NMR δ 139.50, 128.99, 128.03, 85.32, 73.07, 70.46, 56.97, 50.81, 37.19, 28.55, 24.05. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.45; H, 8.99; N, 5.95. Found: C, 71.18; H, 9.06; N, 5.80.

***t*-4-(Benzyloxy)-*t*-2-methoxy-*r*-1-aminocyclohexane (44)**, as a liquid: ^1H NMR δ 7.20–7.42 (m, 5H), 4.56 (s, 2H), 3.26–3.52 (m, 1H), 3.39 (s, 3H), 2.84 (dddd, 1H, J = 11.1, 9.1 and 4.0 Hz), 2.45–2.75 (m, 2H), 1.94–2.20 (m, 2H), 1.78–1.94 (m, 1H), 0.99–1.50 (m, 3H), and see Table 3. ^{13}C NMR δ 139.36, 129.10, 128.25, 83.77, 76.32, 71.04, 57.14, 55.28, 35.89, 31.15, 30.39. Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.45; H, 8.99; N, 5.95. Found: C, 71.29; H, 9.32; N, 6.00.

The crude reaction product (0.152 g) from aziridine **5** was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **25**) afforded pure amino ethers **25** (0.102 g) and **26** (0.040 g).

***t*-4-(Benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-methoxycyclohexane (25)**, as a liquid: IR 1695 cm^{-1} (CO); ^1H NMR δ 7.17–7.48 (m, 5H), 5.74–6.00 (m, 1H), 4.56 and 4.49 (ABdd, 2H, J = 11.9 Hz), 4.09 (q, 2H, J = 7.1 Hz), 3.71–3.90 (m, 1H), 3.55–3.71 (m, 1H), 3.38 (s, 3H), 3.19–3.36 (m, 1H), 1.40–2.25 (m, 6H), 1.24 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.62, 138.95, 128.98, 128.12, 127.95, 74.55, 70.89, 61.09, 56.96, 49.37, 31.77, 30.23, 25.41, 21.80, 15.18. Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.29; H, 8.23; N, 4.62.

***c*-4-(Benzyloxy)-*t*-2-methoxy-*r*-1-[(ethoxycarbonyl)amino]cyclohexane (26)**, as a liquid: IR 1696 cm^{-1} (CO); ^1H NMR δ 7.16–7.46 (m, 5H), 4.64–4.84 (m, 1H), 4.53 and 4.47 (ABdd, 2H, J = 10.8 Hz), 4.11 (q, 2H, J = 7.1 Hz), 3.70–3.85 (m, 1H), 3.49–3.70 (m, 1H), 3.20–3.49 (m, 1H), 3.33 (s, 3H), 1.90–2.24 (m, 2H), 1.52–1.90 (m, 4H), 1.24 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.86, 139.33, 128.93, 128.05, 127.94, 78.67, 73.63, 70.65, 61.27, 56.88, 52.76, 33.83, 28.03, 26.25, 15.15. Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.37; H, 8.11; N, 4.82.

The crude reaction product (0.15 g) from aziridine **6** was subjected to semipreparative TLC (a 7:3 mixture of hexane and ether was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **51**) afforded pure amino ethers **51** (0.102 g) and **52** (0.042 g).

***c*-4-(Benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-methoxycyclohexane (51)**, as a liquid: IR 1695 cm^{-1} (CO); ^1H NMR δ 7.20–7.40 (m, 5H), 4.74 (d, 1H, J = 3.0 Hz), 4.50 and 4.40 (ABdd, 2H, J = 11.9 Hz), 4.03 (q, 2H, J = 7.1 Hz), 3.67–3.85 (m, 1H), 3.50–3.62 (m, 1H), 3.28 (s, 3H), 3.02 (ddd, 1H, J = 8.7 and 3.9 Hz), 2.25–2.42 (m, 1H), 1.55–2.04 (m, 3H), 1.27–1.53 (m, 2H), 1.17 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.98, 139.38, 128.93, 128.09, 128.00, 80.84, 72.78, 70.25, 61.28, 56.58, 50.88, 34.84, 28.41, 24.66, 15.25. Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.12; H, 8.03; N, 4.27.

***t*-4-(Benzyloxy)-*t*-2-methoxy-*r*-1-[(ethoxycarbonyl)amino]cyclohexane (52)**, as a solid, mp 72–73 °C (from hexane): IR 1685 cm^{-1} (CO); ^1H NMR δ 7.20–7.40 (m, 5H), 4.73 (d, 1H, J = 5.8 Hz), 4.58 and 4.53 (ABdd, 2H, J = 11.9 Hz), 4.10 (q, 2H, J = 7.1 Hz), 3.24–3.49 (m, 2H), 3.34 (s, 3H), 2.99 (ddd, 1H, J = 10.6 and 4.1 Hz), 2.53 (dddd, 1H, J = 12.1, 6.5 and 4.1 Hz), 2.16–2.32 (m, 1H), 2.00–2.16 (m, 1H), 1.00–1.50 (m, 3H), 1.24 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 157.22, 139.18, 129.08, 128.20, 128.26, 80.20, 75.67, 70.96, 61.38, 56.53, 55.08, 36.32, 30.87, 28.55, 15.27. Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.29; H, 8.23; N, 4.62.

Methanolysis of Aziridines 5 and 6 in the Presence of $LiClO_4$. General procedure. A solution of the aziridine (0.50 mmol) in anhyd MeOH (2 mL) containing $LiClO_4$ (6 or 16 M solution) was stirred at 70 °C for 2 h. Dilution with ether and evaporation of the washed (water) organic solution afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1 and 2).

Azidolysis of Aziridines 3–8 with NaN_3–NH_4Cl. General procedure. A solution of the aziridine (0.50 mmol) in a 4:1 MeOH–H_2O mixture (4.5 mL) was treated with NaN_3 (0.13 g, 2.0 mmol) and NH_4Cl (0.109 g, 2.0 mmol), and the reaction mixture was stirred for the time and at the temperature shown in the Tables 1 and 2. Dilution with ether and evaporation of the washed (water) ether solution afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1 and 2).

The crude reaction product (0.115 g) from aziridine **3** was subjected to semipreparative TLC (a 6:2:2 mixture of hexane, $CHCl_3$, and Et_3N was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **20**) afforded pure azides **19** (0.065 g) and **20** (0.030 g).

***t*-2-Amino-*t*-4-(benzyloxy)-*r*-1-azidocyclohexane (19)**, as a liquid: IR 2097 cm^{-1} (N_3); ^1H NMR δ 7.10–7.57 (m, 5H), 4.47 (s, 2H), 3.28–3.55 (m, 1H), 2.90–3.15 (m, 1H), 2.55 (dddd, 1H, J = 11.2, 9.4 and 3.9 Hz), 1.92–2.40 (m, 3H), 1.20–1.36 (m, 3H), and see Table 3. ^{13}C NMR δ 139.10, 129.04, 128.24, 128.15, 75.45, 70.97, 68.00, 53.36, 39.79, 30.72, 27.57. Anal. Calcd for $C_{13}H_{18}N_4O$: C, 63.39; H, 7.36; N, 22.75. Found: C, 63.25; H, 7.08; N, 22.81.

***t*-2-Azido-*c*-4-(benzyloxy)-*r*-1-aminocyclohexane (20)**, as a liquid: IR 2098 cm^{-1} (N_3); ^1H NMR δ 7.20–7.44 (m, 5H), 4.53 and 4.47 (ABdd, 2H, J = 11.9 Hz), 3.75–3.89 (m, 1H), 3.39 (dddd, 1H, J = 11.4, 9.7 and 4.2 Hz), 2.56 (ddd, 1H, J = 10.1 and 4.3 Hz), 2.31 (dddd, 1H, J = 13.4, 6.5 and 3.7 Hz), 1.92–2.10 (m, 1H), 1.20–1.92 (m, 4H), and see Table 3. ^{13}C NMR δ 139.21, 129.07, 128.26, 128.08, 73.39, 70.77, 64.94, 55.19, 35.08, 28.95, 28.60. Anal. Calcd for $C_{13}H_{18}N_4O$: C, 63.39; H, 7.36; N, 22.75. Found: C, 63.12; H, 7.22; N, 22.54.

The crude reaction product (0.118 g) from aziridine **4** afforded pure ***t*-2-amino-*c*-4-(benzyloxy)-*r*-1-azidocyclohexane (45)**, as a liquid: IR 2096 cm^{-1} (N_3); ^1H NMR δ 7.14–7.41 (m, 5H), 4.48 (s, 2H), 3.67–3.78 (m, 1H), 2.87–3.08 (m, 2H), 1.97–2.27 (m, 2H), 1.67–1.96 (m, 2H), 1.09–1.54 (m, 2H), and see Table 3. ^{13}C NMR δ 139.30, 129.01, 128.12, 127.98, 72.90, 70.56, 68.62, 50.24, 38.34, 28.75, 25.20. Anal. Calcd for $C_{13}H_{18}N_4O$: C, 63.39; H, 7.36; N, 22.75. Found: C, 63.11; H, 7.29; N, 23.04.

Azidolysis of Aziridines 3–8 with NaN_3–$LiClO_4$ in MeCN. General procedure. A solution of the aziridine (0.50 mmol) in anhyd MeCN (THF in the case of **3** and **4**) (2.0 mL) was treated with NaN_3 (0.13 g, 2.0 mmol) and $LiClO_4$ [$Mg(ClO_4)_2$ or $Zn(OTf)_2$ in the case of **3** and **4**] at the molar concentration as shown in the Tables 1 and 2. The reaction mixture was stirred at 80 °C for the indicated time. Dilution with ether and evaporation of the washed (water) ether solution afforded a crude reaction mixture which was analyzed by ^1H NMR (Tables 1 and 2).

The crude reaction product (0.153 g) from aziridine **5** was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-azidocyclohexane (27)** (0.12 g), as a liquid: IR 2096 (N_3) and 1697 cm^{-1} (CO); ^1H NMR δ 7.15–7.44 (m, 5H), 5.52–5.77 (m, 1H), 4.56 and 4.50 (ABdd, 2H, J = 11.8 Hz), 4.11 (q, 2H, J = 7.0 Hz), 3.42–3.82 (m, 3H), 1.98–2.24 (m, 2H), 1.78–1.98 (m, 1H), 1.41–1.78 (m, 3H), 1.25 (t, 3H, J = 7.0 Hz), and see Table 3. ^{13}C NMR δ 156.57, 139.09, 129.19, 128.41, 128.15, 74.38, 71.18, 61.99, 61.58, 50.73, 33.40, 26.73, 23.59, 15.27. Anal. Calcd for $C_{16}H_{22}N_4O_3$: C, 60.36; H, 6.96; N, 17.60. Found: C, 60.23; H, 7.15; N, 17.81.

The crude reaction product (0.15 g) from aziridine **6** was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-azidocyclohexane (53)** (0.10 g), as a liquid: IR 2096 (N_3) and 1695 cm^{-1} (CO); ^1H NMR δ 7.13–7.34 (m, 5H), 4.68 (d, 1H, J = 8.3 Hz), 4.47 and 4.41 (ABdd, 2H, J = 11.9 Hz), 4.06 (q, 2H, J = 7.1 Hz), 3.59–3.84 (m, 2H), 3.06–3.40 (m, 1H), 2.24 (dddd, 1H, J = 13.7, 6.8 and 4.0 Hz), 1.70–2.04 (m, 3H), 1.26–1.56 (m, 2H), 1.18 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.63, 139.12, 129.03, 128.18, 128.09, 72.53, 70.51, 64.00, 61.62, 50.93, 36.02, 28.64, 25.87, 15.24. Anal. Calcd for $C_{16}H_{22}N_4O_3$: C, 60.36; H, 6.96; N, 17.60. Found: C, 60.12; H, 7.21; N, 17.89.

The crude solid reaction product (0.19 g) from aziridine **7** was recrystallized from hexane to give pure ***t*-4-(benzyloxy)-*t*-2-(tosylamino)-*r*-1-azidocyclohexane (37)** (0.110 g), as a solid, mp 97–98.5 °C: IR 2098 cm^{-1} (N_3); ^1H NMR δ 7.64 (d, 2H, J = 2.9 Hz), 7.10–7.35 (m, 7H), 5.90 (d, 1H, J = 7.4 Hz), 4.47 and 4.33 (ABdd, 2H, J = 11.9 Hz), 3.47–3.66 (m, 2H), 3.24 (sextet, 1H, J = 4.2 Hz), 2.36 (s, 3H), 2.14–2.93 (m, 1H), 1.72–1.89 (m, 1H), 1.41–1.72 (m, 3H), 1.24–1.41 (m, 1H), and see Table 3. ^{13}C NMR δ 144.06, 138.57, 138.46, 130.40, 129.27, 128.58, 128.06, 127.60, 74.06, 71.29, 61.92, 52.43, 31.49, 24.84, 22.23, 21.51. Anal. Calcd for $C_{20}H_{24}N_4O_3S$: C, 59.98; H, 6.04; N, 13.99. Found: C, 60.13; H, 5.79; N, 14.18.

The crude solid reaction product (0.195 g) from aziridine **8** was recrystallized from hexane to give pure ***c*-4-(benzyloxy)-*t*-2-(tosylamino)-*r*-1-azidocyclohexane (59)** (0.17 g), as a solid: mp 103–104 °C; IR 2098 cm^{-1} (N_3); ^1H NMR δ 7.73 (d, 2H, J = 8.3 Hz), 7.07–7.34 (m, 7H), 5.24 (d, 1H, J = 6.7 Hz), 4.30 and 4.24 (ABdd, 2H, J = 11.9 Hz), 3.47–3.60 (m, 1H), 3.17–3.38 (m, 1H), 3.09 (sextet, 1H, J = 4.8 Hz), 2.33 (s, 3H), 2.06–2.24 (m, 1H), 1.58–1.92 (m, 3H), 1.19–1.46 (m, 2H), and see Table 3. ^{13}C NMR δ 144.21, 139.10, 137.77, 130.40, 128.98, 128.15, 127.95, 127.89, 72.24, 70.28, 63.75, 53.50, 36.05, 28.68, 25.81, 22.22. Anal. Calcd for $C_{20}H_{24}N_4O_3S$: C, 59.98; H, 6.04; N, 13.99. Found: C, 59.83; H, 6.20 ; N, 14.31.

Azidolysis of Aziridines 5–8 with NaN_3 in DMF. General procedure. A solution of the aziridine (0.50 mmol) in anhyd DMF (2.0 mL) containing NaN_3 (0.13 g, 2.0 mmol) was stirred at rt for the time indicated in the Tables 1 and 2. Dilution with water, extraction with ether, and evaporation of the washed (water) ether extracts afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1 and 2).

The crude reaction product (0.15 g) from aziridine **5** was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the most intense band afforded pure ***t*-2-azido-*c*-4-(benzyloxy)-*r*-1-[(ethoxycarbonyl)amino]cyclohexane (28)** (0.11 g), as a liquid: IR 2096 (N_3) and 1698 cm^{-1} (CO); ^1H NMR δ 7.18–7.44 (m, 5H), 4.72 (d, 1H, J = 6.8 Hz), 4.52 and 4.47 (ABdd, 2H, J = 11.9 Hz), 4.14 (q, 2H, J = 7.1 Hz), 3.73–3.85 (m, 1H), 3.40–3.66 (m, 2H), 2.20–2.40 (m, 1H), 1.80–2.07 (m, 2H), 1.40–1.80 (m, 3H), 1.26 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.88, 139.10, 129.16, 128.38, 128.15, 72.93, 70.88, 61.76, 61.18, 54.33, 35.42, 28.52, 27.41, 15.30. Anal. Calcd for $C_{16}H_{22}N_4O_3$: C, 60.36; H, 6.96; N, 17.60. Found: C, 60.31; H, 7.02; N, 17.71.

The crude reaction product (0.19 g) from aziridine **7** was recrystallyzed from hexane to give pure ***t*-2-azido-*c*-4-(benzyloxy)-*r*-1-(tosylamino)cyclohexane (38)** (0.17 g) as a semisolid: IR 2102 cm^{-1} (N_3); ^1H NMR δ 7.73 (d, 2H, J = 8.2 Hz), 7.08–7.35 (m, 5H), 4.79 (d, 1H, J = 6.9 Hz), 4.41 and 4.34 (ABdd, 2H, J = 11.9 Hz), 3.59–3.70 (m, 1H), 3.30–3.50 (m, 1H), 2.84–3.04 (m, 1H), 2.34 (s, 3H), 2.05–2.21 (m, 1H), 1.12–1.90 (m, 5H), and see Table 3. ^{13}C NMR δ 144.15, 138.92, 138.22, 130.31, 129.10, 128.33, 128.08, 127.77, 72.47, 70.80, 60.66, 57.11, 35.31, 30.34, 28.14, 27.79, 22.20. Anal. Calcd for $C_{20}H_{24}N_4O_3S$: C, 59.98; H, 6.04; N, 13.99. Found: C, 59.75; H, 6.39; N, 13.69.

Azidolysis of Aziridine 3 with NaN_3–H_2SO_4. A solution of aziridine **3** (0.101 g, 0.50 mmol) in acetone (2 mL) containing NaN_3 (0.260 g, 4.0 mmol) was treated dropwise under stirring with aqueous 4 N H_2SO_4 until the reaction mixture was slightly acid. Stirring was prolonged for 18 h at rt. Dilution with water, extraction with ether, and evaporation of the washed (saturated aqueous $NaHCO_3$ and water) afforded a crude reaction product (0.060 g) which was analyzed by ^1H NMR (Table 1).

Aminolysis of Aziridines 5, 6, and 8 with Et_2NH–EtOH. General procedure. A solution of the aziridine (0.50 mmol) in EtOH (2.0 mL) containing Et_2NH (0.15 mL, 1.5 mmol) was stirred at 80 °C for 24 h (4 days in the case of **6**); after cooling, the solution was diluted with ether, and evaporation of the washed (water) ether solution afforded a crude reaction product which was analyzed by ^1H NMR (Tables 1 and 2).

The crude reaction product (0.124 g) from aziridine **5** was subjected to semipreparative TLC (an 8:2:0.1 mixture of hexane, ether, and Et_3N was used as the eluant). Extraction of the most intense band afforded pure ***c*-4-(benzyloxy)-*t*-2-(*N*,*N*-diethylamino)-*r*-1-[(ethoxycarbonyl)amino]cyclohexane (30)** (0.090 g) as a liquid: IR 1720 cm^{-1} (CO); ^1H NMR δ 7.16–7.38 (m, 5H), 5.50–5.76 (m, 1H), 4.51 and 4.46 (ABdd, 2H, J = 12.1 Hz), 4.10 (q, 2H, J = 7.1 Hz), 3.75–3.87 (m, 1H), 3.20–3.40 (m, 1H), 2.85–3.10 (m, 1H), 2.63 (sextet, 2H, J = 7.0 Hz), 2.20–2.42 (m, 3H), 2.10 (dddd, 1H, J = 13.3, 5.9 and 3.0 Hz), 1.86–2.03 (m, 1H), 1.15–1.70 (m, 3H), 1.24 (t, 3H, J = 7.1 Hz), 1.05 (t, 6H, J = 7.0 Hz), and see Table 3. ^{13}C NMR δ 157.72, 139.67, 129.01, 128.03, 127.89, 73.86, 70.56, 61.09, 57.37, 52.41, 43.83, 30.38, 28.79, 28.00, 15.39, 15.03. Anal.

Calcd for $C_{20}H_{32}N_2O_3$: C, 68.93; H, 9.25; N, 8.04. Found: C, 68.77; H, 9.31; N, 7.88.

The crude reaction product (0.14 g) from aziridine **6** was subjected to semipreparative TLC (an 8:2:0.1 mixture of hexane, ether, and Et_3N was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **56**) afforded pure amines **55** (0.035 g) and **56** (0.086 g).

***c*-4-(Benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-(*N,N*-diethylamino)cyclohexane (55)**, a semisolid: IR 1689 cm^{-1} (CO) ; ^1H NMR δ 7.16–7.43 (m, 5H), 5.51–5.69 (m, 1H), 4.65 and 4.45 (ABdd, 2H, J = 12.1 Hz), 4.09 (q, 2H, J = 7.1 Hz), 3.59–3.80 (m, 2H), 2.85–3.03 (m, 1H), 2.64 (sextet, 2H, J = 7.1 Hz), 2.21–2.56 (m, 3H), 1.91–2.11 (m, 1H), 1.54–1.73 (m, 2H), 1.24 (t, 3H, J = 7.1 Hz), 1.12–1.40 (m, 2H), 1.02 (t, 6H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 157.68, 139.65, 128.95, 128.17, 127.95, 72.81, 70.15, 63.23, 61.07, 47.62, 43.94, 36.06, 30.75, 18.80, 15.38, 15.09. Anal. Calcd for $C_{20}H_{32}N_2O_3$: C, 68.93; H, 9.25; N, 8.04. Found: C, 68.71; H, 9.24; N, 8.12.

***t*-4-(Benzyloxy)-*t*-2-(*N,N*-diethylamino)-*r*-1-[(ethoxycarbonyl)amino]cyclohexane (56)**, a solid, mp 58–59 °C: IR 1714 cm^{-1} (CO) ;^1H NMR δ 7.12–7.40 (m, 5H), 5.32–5.57 (m, 1H), 4.49 and 4.44 (ABdd, 2H, J = 12.0 Hz), 4.02 (q, 2H, J = 7.1 Hz), 3.10–3.44 (m, 2H), 2.47–2.74 (m, 3H), 2.00–2.47 (m, 5H), 1.11–1.48 (m, 3H), 1.16 (t, 3H, J = 7.1 Hz), 0.94 (t, 6H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 157.81, 139.56, 129.08, 128.21, 77.47, 71.00, 61.47, 61.12, 52.20, 44.00, 31.09, 30.72, 29.87, 15.36, 15.23. Anal. Calcd for $C_{20}H_{32}N_2O_3$: C, 68.93; H, 9.25; N, 8.04. Found: C, 69.19; H, 9.51; N, 7.95.

The crude reaction product (0.21 g) from aziridine **8** was subjected to semipreparative TLC (a 7:3:0.2 mixture of hexane, AcOEt and Et_3N was used as the eluant). Extraction of the two most intense bands (the faster moving band contained **62**) afforded pure amines **61** (0.052 g) and **62** (0.14 g).

***c*-4-(Benzyloxy)-*t*-2-(tosylamino)-*r*-1-(*N,N*-diethylamino)cyclohexane (61)**, a solid, mp 94–96.5 °C (from hexane): ^1H NMR δ 7.74 (d, 2H, J = 8.2 Hz), 7.22–7.47 (m, 5H), 7.21 (d, 2H, J = 8.2 Hz), 4.56 and 4.45 (ABdd, 2H, J = 12.0 Hz), 3.63–3.75 (m, 1H), 3.09 (ddd, 1H, J = 10.7 and 3.8 Hz), 2.91 (dddd, 1H, J = 13.8, 6.4 and 3.2 Hz), 2.29–2.49 (m, 1H), 2.39 (s, 3H), 2.17 (q, 4H, J = 6.9 Hz), 1.91–2.07 (m, 1H), 1.25–1.63 (m, 4H), 0.86 (t, 6H, J = 6.9 Hz), and see Table 3. ^{13}C NMR δ 143.85, 139.55, 136.75, 130.14, 128.95, 128.01, 127.81, 72.86, 70.20, 62.83, 49.44, 43.02, 36.09, 30.30, 22.17, 18.68, 14.74. Anal. Calcd for $C_{24}H_{34}N_2O_3S$: C, 66.94; H, 7.96; N, 6.50. Found: C, 67.10; H, 8.21; N, 6.42.

***t*-4-(Benzyloxy)-*t*-2-(*N,N*-diethylamino)-*r*-1-(tosylamino)cyclohexane (62)**, a solid, mp 115–117 °C: ^1H NMR δ 7.75 (d, 2H, J = 8.2 Hz), 7.11–7.40 (m, 7H), 4.54 and 4.48 (ABdd, 2H, J = 11.7 Hz), 3.31 (ddd, 1H, J = 14.7, 10.6 and 4.1 Hz), 2.64 (ddd, 1H, J =10.2 and 3.9 Hz), 2.42 (s, 3H), 2.00–2.56 (m, 8H), 1.01–1.40 (m, 3H), 0.88 (t, 6H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 143.94, 139.18, 137.33, 130.19, 129.02, 128.20, 128.15, 127.83, 76.86, 70.88, 60.88, 53.53, 43.05, 30.60, 30.37, 29.33, 22.14, 14.75. Anal. Calcd for $C_{24}H_{34}N_2O_3S$: C, 66.94; H, 7.96; N, 6.50. Found: C, 66.80; H, 8.32; N, 6.72.

Aminolysis of Aziridines 5, 6, and 8 with Et_2NH–$LiClO_4$ in MeCN. A solution of the aziridine (0.50 mmol) in anhyd MeCN (2.0 mL) was treated with $NHEt_2$ (0.15 mL, 1.5 mmol) and $LiClO_4$ (0.42 g, 4.0 mmol), and the reaction mixture was stirred at the temperature and for the time shown in the Tables 1 and 2. Dilution with ether and evaporation of the washed (water) ether solution afforded a crude product which was analyzed by ^1H NMR (Tables 1 and 2).

The crude solid reaction product (0.17 g) from **5** was recrystallized from hexane to give pure ***t*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-(*N,N*-diethylamino)cyclohexane (29)** (0.15 g) as a solid, mp 47–48 °C: IR 1684 cm^{-1} (CO) ; ^1H NMR δ 7.20–7.40 (m, 5H), 5.40–5.58 (m, 1H), 4.58 and 4.51 (ABdd, 2H, J = 11.9 Hz), 4.11 (q, 2H, J = 7.1 Hz), 3.17–3.53 (m, 2H), 2.87–3.07 (m, 1H), 2.56 (sextet, 2H, J = 7.1 Hz), 2.21–2.46 (m, 3H), 2.01–2.21 (m, 1H), 1.75–1.91 (m, 1H), 1.10–1.43 (m, 3H), 1.25 (t, 3H, J = 7.1 Hz), 0.99 (t, 6H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 157.58, 139.39, 128.96, 128.15, 128.06, 75.71, 70.83, 62.80, 61.07, 50.19, 43.74, 38.52, 31.96, 20.67, 15.32, 15.18. Anal. Calcd for $C_{20}H_{32}N_2O_3$: C, 68.93; H, 9.25; N, 8.04. Found: C, 69.06; H, 9.17; N, 8.33.

Reaction of Aziridines 3–8 with PhSH–Et_3N (Corey's Protocol). The following procedure is typical.[14] A solution of the aziridine **5** (0.50 mmol) in MeOH (0.5 mL) was treated with Et_3N (0.28 mL, 2.8 mmol) and PhSH (0.14 mL, 1.50 mmol), and the reaction mixture was stirred for 18 h at rt. Dilution with ether and evaporation of the washed (saturated aqueous $NaHCO_3$ and water) ether extracts afforded a crude reaction product (0.19 g) which was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-4-(benzyloxy)-*t*-2-(phenylthio)-*r*-1-[(ethoxycarbonyl)amino]cyclohexane (32)** (0.17 g) as a liquid: IR 1710 cm^{-1} (CO); ^1H NMR δ 7.44–7.63 (m, 2H), 7.11–7.44 (m, 8H), 4.82 (d, 1H, J = 7.6 Hz), 4.45 (s, 2H), 4.12 (q, 2H, J = 7.1 Hz), 3.60–3.74 (m, 1H), 3.40–3.60 (m, 1H), 3.34 (ddd, 1H, J = 10.1 and 3.4 Hz), 2.19–2.38 (m, 1H), 1.93–2.12 (m, 1H), 1.35–1.93 (m, 4H), 1.24 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.66, 139.30, 134.01, 133.69, 129.56, 129.03, 128.18, 128.03, 73.22, 70.60, 61.45, 53.55, 47.91, 36.97, 28.86, 28.55, 15.29. Anal. Calcd for $C_{22}H_{27}NO_3S$: C, 68.54; H, 7.06; N, 3.63. Found: C, 68.68; H, 7.30; N, 3.97.

The crude reaction product (0.152 g) from aziridine **3** consisted of a mixture of thioethers **21** and **22** which did not separate under any TLC conditions. As a consequence, pure **21** (0.058 g) and **22** (0.057 g) (after semipreparative TLC) were obtained by deprotection of the corresponding urethanes **31** (0.10 g) and **32** (0.10 g) (see later).

***t*-2-Amino-*t*-4-(benzyloxy)-*r*-1-(phenylthio)cyclohexane (21)**, a liquid: ^1H NMR δ 7.39–7.53 (m, 2H), 7.17–7.39 (m, 8H), 4.53 (s, 2H), 3.28–3.47 (m, 1H), 2.51–2.71 (m, 2H), 2.31–2.47 (m, 1H), 2.00–2.20 (m, 2H), 1.20–1.47 (m, 3H), and see Table 3. ^{13}C NMR δ 139.41, 139.35, 134.10, 134.04, 129.62, 129.07, 128.21, 76.05, 70.86, 56.76, 52.75, 41.37, 32.65, 30.74. Anal. Calcd for $C_{19}H_{23}NOS$: C, 72.80; H, 7.39; N, 4.47. Found: C, 72.76; H, 7.55; N, 4.41.

***c*-4-(Benzyloxy)-*t*-2-(phenylthio)-*r*-1-aminocyclohexane (22)**, a liquid: ^1H NMR δ 7.35–7.50 (m, 2H), 7.08–7.35 (m, 8H), 4.36 (s, 2H), 3.51–3.61 (m, 1H), 3.10–3.28 (m, 1H), 2.54–2.73 (m, 1H), 2.16–2.37 (m, 1H), 1.66–2.04 (m, 3H), 1.18–1.45 (m, 2H), and see Table 3. ^{13}C NMR δ 139.32, 134.41, 134.30, 129.62, 129.01, 128.36, 128.11, 128.06, 73.32, 70.49, 53.82, 50.51, 37.29, 30.36, 28.95. Anal. Calcd for $C_{19}H_{23}NOS$: C, 72.80; H, 7.39; N, 4.47. Found: C, 72.54; H, 7.40; N, 4.65.

The crude reaction product (0.154 g) from aziridine **4** was subjected to semipreparative TLC (a 7:3:1 mixture of hexane, AcOEt, and Et_3N was used as the eluant). Extraction of the most intense band afforded pure ***c*-4-(benzyloxy)-*t*-2-amino-*r*-1-(phenylthio)cyclohexane (47)** (0.13 g), as a liquid: ^1H NMR δ 7.37–7.55 (m, 2H), 7.12–7.37 (m, 8H), 4.44 (s, 2H), 3.69–3.81 (m, 1H), 3.06 (ddd, 1H, J = 10.5 and 3.7 Hz), 2.72 (ddd, 1H, J = 9.9 and 5.5 Hz), 2.64 (dddd, 1H, J = 13.6, 6.1 and 3.6 Hz), 1.75–2.09 (m, 3H), 1.19–1.53 (m, 2H), and see Table 3. ^{13}C NMR δ 139.46, 134.59, 133.81, 129.51, 129.01, 128.93, 128.18, 127.98, 127.88, 73.49, 70.33, 57.06, 49.66, 39.55, 30.28, 28.14. Anal. Calcd for $C_{19}H_{23}NOS$: C, 72.80; H, 7.39; N, 4.47. Found: C, 72.59; H, 7.12; N, 4.19.

The crude reaction product (0.19 g) from aziridine **6** was subjected to semipreparative TLC (a 6:4 mixture of hexane and ether was used as the eluant). Extraction of the most intense band afforded pure ***c*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-(phenylthio)cyclohexane (57)** (0.148 g), as a solid, mp 103–104 °C (from hexane): IR 1687 cm^{-1} (CO); ^1H NMR δ 7.40–7.55 (m, 2H), 7.12–7.40 (m, 8H), 4.90 (d, 1H, J = 7.6 Hz), 4.52 and 4.43 (ABdd, 2H, J = 11.9 Hz), 4.09 (q, 2H, J = 7.1 Hz), 3.75–3.95 (m, 1H), 3.63–3.75 (m, 1H), 2.94–3.18 (m, 1H), 2.35–2.52 (m, 1H), 1.78–2.02 (m, 3H), 1.37–1.63 (m, 2H), 1.22 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.56, 139.29, 134.44, 133.66, 129.68, 129.50, 128.93, 128.09, 128.01, 127.92, 127.77, 73.02, 70.25, 61.37, 51.74,

(14) Crotti, P.; Giovani, E.; Macchia, F.; Pineschi, M. *Synlett* **1992**, 303, and references therein.

50.81, 36.81, 30.07, 28.00, 15.24. Anal. Calcd for $C_{22}H_{27}NO_3S$: C, 68.54; H, 7.06; N, 3.63. Found: C, 68.71; H, 7.00; N, 3.49.

The crude reaction product (0.228 g) from aziridine **7** afforded practically pure ***c*-4-(benzyloxy)-*t*-2-(phenylthio)-*r*-1-(tosylamino)cyclohexane** (**40**) (0.22 g), as a viscous liquid: ^{1}H NMR δ 7.66 (d, 2H, J = 8.3 Hz), 7.02–7.30 (m, 12 H), 5.16 (d, 1H, J = 4.3 Hz), 4.36 and 4.31 (ABdd, 2H, J = 12.1 Hz), 3.47–3.59 (m, 1H), 2.98 (ddd, 1H, J = 9.2 and 3.7 Hz), 2.96 (sextet, 1H, J = 4.4 Hz), 2.35 (s, 3H), 1.93–2.20 (m, 2H), 1.27–1.79 (m, 4H), and see Table 3. ^{13}C NMR δ 144.03, 139.18, 138.14, 133.75, 132.94, 130.31, 129.67, 129.02, 128.41, 128.18, 128.03, 127.92, 72.93, 70.59, 55.34, 47.87, 36.40, 28.25, 28.09, 22.23. Anal. Calcd for $C_{26}H_{29}NO_3S_2$: C, 66.76; H, 6.25; N, 2.99. Found: C, 66.43; H, 6.41; N, 3.17.

The crude solid reaction product (0.23 g) from aziridine **8** was recrystallized from hexane to give pure ***c*-4-(benzyloxy)-*t*-2-(tosylamino)-*r*-1-(phenylthio)cyclohexane** (**63**) (0.21 g), as a solid, mp 128–130 °C: ^{1}H NMR δ 7.72 (d, 2H, J = 8.0 Hz), 7.05–7.40 (m, 12H), 5.47 (d, 1H, J = 4.4 Hz), 4.43 and 4.36 (ABdd, 2H, J = 11.8 Hz), 3.57–3.70 (m, 1H), 3.34 (sextet, 1H, J = 4.2 Hz), 2.99 (ddd, 1H, J = 8.4 and 4.1 Hz), 2.42–2.61 (m, 1H), 2.40 (s, 3H), 1.64–2.01 (m, 3H), 1.40–1.62 (m, 2H), and see Table 3. ^{13}C NMR δ 144.09, 139.27, 137.23, 133.55, 130.33, 129.56, 128.90, 128.15, 128.00, 127.86, 72.87, 70.22, 52.92, 51.40, 36.37, 29.74, 27.57, 22.17. Anal. Calcd for $C_{26}H_{29}NO_3S_2$: C, 66.76; H, 6.25; N, 2.99. Found: C, 66.91; H, 6.37; N, 2.73.

Reaction of Aziridines 3–8 with PhSH–$LiClO_4$ in MeCN. General procedure. A solution of the aziridine (0.50 mmol) in anhyd MeCN (THF in the case of **3** and **4**) (2.0 mL) was treated with PhSH (0.14 mL, 1.5 mmol) and $LiClO_4$ (0.42 g, 4.0 mmol) [$Mg(ClO_4)_2$ (0.223 g, 1.0 mmol) in the case of **3** and **4**], and the reaction mixture was stirred at 80 °C for the time shown in the Tables 1 and 2. The usual workup afforded a crude reaction product which was analyzed by ^{1}H NMR (Tables 1 and 2).

The crude solid reaction product (0.19 g) from aziridine **5** was recrystallized from hexane to give pure ***t*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-(phenylthio)cyclohexane** (**31**) (0.18 g), as a solid, mp 96–98 °C: IR 1711 cm^{-1} (CO); ^{1}H NMR δ 7.40–7.53 (m, 2H), 7.13–7.40 (m, 8H), 5.95 (d, 1H, J = 6.6 Hz), 4.56 and 4.49 (ABdd, 2H, J = 11.9 Hz), 4.10 (q, 2H, J = 7.1 Hz), 3.70–3.88 (m, 1H), 3.56–3.70 (m, 1H), 3.26–3.41 (m, 1H), 2.12–2.45 (m, 2H), 1.80–2.03 (m, 1H), 1.41–1.78 (m, 3H), 1.23 (t, 3H, J = 7.1 Hz), and see Table 3. ^{13}C NMR δ 156.47, 138.95, 135.05, 132.11, 129.62, 129.12, 128.30, 128.09, 127.52, 74.70, 71.06, 61.31, 50.85, 48.97, 33.69, 27.65, 24.68, 15.31. Anal. Calcd for $C_{22}H_{27}NO_3S$: C, 68.54; H, 7.06; N, 3.63. Found: C, 68.56; H, 6.91; N, 3.55.

The crude solid reaction product (0.23 g) from aziridine **7** was recrystallized from hexane to give pure ***t*-4-(benzyloxy)-*t*-2-(tosylamino)-*r*-1-(phenylthio)cyclohexane** (**39**) (0.18 g), as a solid, mp 132–134 °C: ^{1}H NMR δ 7.74 (d, 2H, J = 8.3 Hz), 7.05–7.34 (m, 12H), 6.23 (d, 1H, J = 7.2 Hz), 4.48 and 4.36 (ABdd, 2H, J = 12.0 Hz), 3.59 (quintet, 1H, J = 3.4 Hz), 3.28–3.45 (m, 2H), 2.34 (s, 3H), 2.14–2.36 (m, 1H), 2.06 (ddd, 1H, J = 14.6 and 3.5 Hz), 1.63–1.80 (m, 2H), 1.30–1.63 (m, 2H), and see Table 3. ^{13}C NMR δ 143.71, 138.58, 134.73, 131.70, 130.25, 129.74, 129.22, 129.04, 128.49, 128.06, 127.63, 127.57, 74.29, 71.20, 52.26, 48.77, 30.90, 25.31, 22.19, 22.01. Anal. Calcd for $C_{26}H_{29}NO_3S_2$: C, 66.76; H, 6.25; N, 2.99. Found: C, 66.64; H, 6.01; N, 3.21.

General Procedure for Deprotection of the Urethanes.[13] A solution of the urethane (0.25 mol) in a 1:1 mixture of ethylene glycol and aqueous 2 N KOH was stirred at 100 °C for 18 h (two days in the case of compounds **31** and **32**). Dilution with ether and evaporation of the washed (water) ether solution afforded the corresponding pure *N*-unprotected derivative.

Reaction of Aziridine 5 with *p*-Toluenesulfonic Acid. A solution of the aziridine **5** (0.069 g, 0.25 mmol) in $CHCl_3$ (2.0 mL) was treated at −30 °C (or at rt) with *p*-toluenesulfonic acid (0.052 g, 0.30 mmol), and the reaction mixture was stirred for 10 min at the same temperature. Evaporation of the washed (water) organic solution afforded pure ***t*-4-(benzyloxy)-*t*-2-[(ethoxycarbonyl)amino]-*r*-1-tosyloxycyclohexane** (**33**) (0.109 g), as a solid, mp 137–139 °C (from hexane): IR 1689 cm^{-1} (CO); ^{1}H NMR δ 7.82 (d, 2H, J = 8.2 Hz), 7.18–7.42 (m, 7H), 5.72 (m, 1H), 4.45–4.63 (m, 1H), 4.54 and 4.47 (ABdd, 2H, J = 11.9 Hz), 4.05 (q, 2H, J = 7.0 Hz), 3.59–3.80 (m,2H), 2.45 (s, 3H), 1.79–2.25 (m, 3H), 1.50–1.79 (m, 3H), 1.21 (t, 3H, J = 7.0 Hz), and see Table 3. ^{13}C NMR δ 156.35, 145.38, 138.74, 134.74, 130.54, 129.19, 128.43, 128.12, 80.13, 74.00, 71.28, 61.48, 49.82, 32.53, 25.93, 24.17, 22.37, 15.26. Anal. Calcd for $C_{23}H_{29}NO_6S$: C, 61.73; H, 6.53; N, 3.13. Found: C, 61.99; H, 6.68; N, 3.20.

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